COHERENT GAMMA-RAY SCATTERING AND TRANSMISSION MEASUREMENTS
IN BONE DENSITOMETRY

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A thesis submitted to the University of Surrey
for the degree of

DOCTOR OF PHILOSOPHY

OCTOBER, 1988
Dedicated to my parents
ABSTRACT

Two different methods of measuring bone mineral content: gamma-ray scattering and gamma-ray transmission tomography have been studied using simple tissue substitute materials.

Elastic photon scattering, as currently employed, relies on taking the ratio of the coherent and incoherent (Compton) scattering intensities to correct for beam attenuation. An alternative method of correction, using transmission measurements as for Compton scattering densitometry, was explored. It was demonstrated that for the 60 KeV gamma-ray from $^{241}$Am coherent scattering, corrected in this way, was more sensitive to variations in the bone phantoms than the coherent to Compton ratio for a given dose. The improvement was probably not sufficient, however, to warrant the more complicated measurement procedure required.

A first generation gamma-ray transmission tomography scanner was constructed and revealed significant differences (up to 7%) between the true linear attenuation coefficients and those estimated from tomographs. This was due to photon scattering which contributed to the measured flux giving artificially high count rates. By employing a narrow, well collimated interrogating beam and maintaining a constant detector and source geometry it was still possible to characterise the phantoms using the empirically derived attenuation coefficients as, under these conditions, they were still functions of the material only. With most modern scanners using fan beam geometries of some form the influence of photon scattering will probably be even greater than on the simple system employed in this work.
Experiments were also done using a $^{153}$Gd isotopic source to produce dual energy measurements using potassium hydrogen phosphate ($\text{K}_2\text{HPO}_4$) as a reference material. The results were in agreement with other work published in the literature using dual energy X-ray scans showing greater accuracy in bone mineral estimation albeit with some loss of precision.
ACKNOWLEDGEMENTS

I would like to thank those involved in my supervision: Stephen Kerr who initiated the work, Nicholas Spyrou who took over the reins from him, and Professor Daphne Jackson who looked after all three of us. The advice received from David Bradley and Professor Ghose was also greatly appreciated.

My thanks also go to Brian Torr who designed the tomography scanner and to Harvey Harrison who built the counting electronics. The experimental work was only made possible by the abilities of Messrs. Bristow, Scherrer and Willoughby in the mechanical workshops who built all the experimental apparatus turning many a rough sketch into real hardware. Neil McCuaig provided considerable assistance in the use of the reconstruction and analysis package on the PRIME and advice on tomography in general. I would also like to mention the technical support received from Judd Hawkins, especially in looking after the germanium detector, and to thank Dave Voss and Adrienne Gilmour who always had a great concern for my safety.

The Gd-153 source was kindly lent to me by Michael Hayes of the BP Research Centre, Sunbury, and the Am-241 was made available by Amersham International.

I am grateful to many members of the Physics Department at Surrey who have listened patiently to my ramblings and made many useful comments and suggestions but I feel Ian Holloway deserves a special mention.

There are a number of friends who have provided help and encouragement and it is with pleasure that I thank Alison Turner, Andy Parratt, Richard Tookey, Catherine Taylor and Zoe Rippengal.

Financial support was provided by the SERC in the form of a quota studentship.
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INTRODUCTION

In elderly people, especially post-menopausal women, there is a marked decline in the amount of new bone tissue being formed compared with the amount being resorbed. This leads to a nett loss in total bone mass, a syndrome known as osteoporosis. It is generally recognised that this thinning of the bones contributes to the increase in fracture risk found in older sections of the population. The cost of these fractures is significant not only in terms of personal suffering but also in terms of health care resources. Woolf (WOO 87) quotes that 18% of orthopaedic beds in the UK are occupied by patients with proximal femur fractures, a common result of osteoporotic weakening of bone and one with a 15% mortality. Similar figures are to be found in the literature for other developed countries e.g. the USA (RIG 86).

For these reasons there has been a considerable interest in recent years in methods of diagnosis, treatment and, ideally, prevention of osteoporosis. One of the most useful diagnostic aids being techniques to estimate the bone mass, or density, in the hope of identifying the onset of significant bone loss in individuals prior to the development of serious fractures (AIT 84). There is still, however, much debate as to which method is the most appropriate and on the suitability of the different skeletal sites as indicators of likely fracture risk. This thesis concerns two possible bone densitometry techniques: gamma-ray scattering and transmission tomography.
1.1 Introduction

Bone is one of the body's connective tissues, its distinctive feature being its rigidity, a result of the hydroxyapatite mineral deposited on the protein framework. The skeleton of an adult male makes up 13-14% of the total body weight i.e. about 9Kg for a 65Kg man (BIG 76), of which 5.5Kg will be actual bone tissue the remainder being the bone marrow. The primary role of bone is mechanical but it is also important biochemically, with 99% of the body's calcium and 50% of its magnesium being stored in the skeleton. Some trace elements, such as sodium, are also present in the bones but it is not clear if they are available to the body's metabolism or are merely trapped in the bone matrix.

1.2 Bone Composition and Structure

The skeleton acts as a physical framework to support the body and to provide protection for the more delicate organs such as the brain. It also acts as a series of rigid, jointed levers allowing the muscles to operate effectively and to enable motion. Not all the mechanical functions are structural (the small bones in the middle ear for example are used to transmit and amplify sound waves) however those bones that do have to support the body are subjected to very high stresses. As an example the femoral neck may experience a load of up to six times body weight and in
a young adult is actually capable of withstanding a vertical force equivalent to almost 1 tonne. This compressive strength is due to the mineral phase present, the collagen fibres that make up most of the organic part of the bones provide tensile strength. It is not only the intrinsic properties of the bone tissue that are important, however, but also the physical arrangement of this tissue. The long bones for instance are effectively hollow, cylindrical tubes of hard bone with a reinforcing network of strands, or trabeculae, at the ends. It is found that bone tends to become thicker at points of stress and thinner in those areas where the loads are less. Thus it models itself to the optimum architecture for a given role.

1.2.1 Extra-Cellular Components of Bone

The non-cellular constituents of bone make up some 97% of its volume and can be considered as an organic matrix with a mineral phase embedded in it.

1.2.1.1 Organic Matrix

Approximately 25% of the weight of adult bone is the organic matrix or osteoid. Of this 95% is collagen; a tough, fibrous protein found also in tendons and the skin. The remaining 5% is a mucopolysaccharide which has no clear purpose though it has been suggested it may play a role in the calcification of bone or act as a lubricant to facilitate some degree of relative motion of the mineralised fibres when the bone is stressed.
Fig. 1.1 Longitudinal section of a human femoral head showing both trabecular and cortical bone.
(From Vaughan, 1981, "Physiology of Bone", OUP, Oxford)
1.2.1.2 Bone Mineral

The mineral portion of bone is made up of an amorphous calcium phosphate and a crystalline form similar to hydroxyapatite \((\text{Ca}_{10}\text{(PO}_4)_6\text{(OH)}_2)\): the relative proportions of one to the other vary but are roughly 40% amorphous to 60% crystalline. The crystal size is approximately 60nm x 5nm but can grow up to 600nm in the elderly (AIT 84). Ratios of calcium to phosphorous are not constant within bones due to the amorphous phosphate being present in variable quantities and not having a fixed chemical composition.

Other elements are found in trace quantities either as substitutionary ions within the crystal e.g. fluorine (giving rise to calcium fluoroapatite), strontium, lead and radium; or adsorbed onto the crystal surface e.g. magnesium, potassium and zinc.

The surface ions of the lattice are hydrated giving rise to a bound layer of water called the hydration shell and it is through this interface that ions are exchanged between the mineral and the extra-cellular fluid.

The details of the process of mineralisation are not understood. Calcium and phosphate ions are present in the tissue fluids and the collagen fibres appear to act as a nucleation site but the role that the bone cells may play is not known. The calcification itself is rapid with 70% of a collagen fibre being
mineralised within 4 days, initially by amorphous phosphate, with crystallisation following more slowly with the crystals aligning themselves along the fibre. Collagen, as has been mentioned, is found elsewhere in the body but does not normally calcify due to the inhibitory effects of inorganic pyro-phosphate (PP1). In bones however local PP1 is destroyed by alkaline phosphatase thus allowing the precipitation of calcium phosphate.

1.2.2 Bone Cells

There are three cell types to be found in bone tissue and it is these that control its metabolic processes.

1.2.2.1 Osteoblasts

The osteoblasts are derived from mesenchymal progenitor cells that are found on all bone surfaces an they are responsible for the laying down of new bone. At growth or repair sites they enlarge and form a pseudo-epithelium covering the bone surface. They then secrete mucopolysaccharide, alkaline phosphotase (thus enabling calcium phosphate formation) and tropocollagen. The tropocollagen molecules link up to form the collagen fibres which then order themselves; either as parallel bunches or as an interweaving network. As has been discussed, the subsequent mineralisation of this protein proceeds very rapidly.
1.2.2.2 Osteocytes

Osteoblasts may become trapped in the osteoid in hollows called lacunae and are then known as osteocytes. These cells are connected to their neighbours by cytoplasmic processes that pass through the canaliculi permeating the bone. In this way there is a layer of cells over all the bone surfaces thus producing a local extra-cellular fluid. The shape of osteocytes in lamellar bone tends to be flattened with the orientation parallel to the layers of osseous tissue but in woven bone they are round and more closely packed.

There is evidence that osteocytes control the mineralisation of bone as the lacunae are found to enlarge following excessive levels of vitamin D or parathyroid hormone (both stimulators of bone resorption). This process is known as osteocytic osteolysis or lacunar resorption.

The osteocyte seems to be important for bone health and maintenance: tissue with dead osteocytes is gradually replaced with new, living bone.

1.2.2.3 Osteoclasts

Osteoclasts are derived from mono-nuclear, haemopoetic cells, believed to be from the red bone marrow, but are themselves multi-nucleated having 10 to 20 nuclei (though large ones may have in excess of 100). These cells are responsible for
the resorption of the bone and are highly mobile, moving from site to site over the bone surface leaving pits called Howship’s lacunae. At the resorption interface the osteoclast extends finger-like projections of cytoplasm towards the bone giving a ruffled border. Micrographs also show a brush-like border believed to be produced by strands of demineralised collagen.

The mechanism of resorption is still being investigated. It is believed that the mineral component is removed first by the action of lactic and citric acids or enzymes such as acid phosphatase that are present in the osteoclasts. The remaining demineralised collagen is then eaten away by a collagenase produced either by the osteoclast or, perhaps, by other, mono-nuclear cells that attack the bone when the osteoclast moves away. While the detailed process is still not clear it is certain that the osteoclast is the cell responsible for bone catabolism.

1.2.2.4 Bone Remodelling

Bone tissue is in a state of dynamic equilibrium, with osteoclasts resorbing bone and a closely coupled process of resynthesis being conducted by the osteoblasts. The resulting turnover of the bone tissue is about 3-5% per annum in adults and somewhat higher in growing children. This process is carried out at discrete foci known as remodelling units and in cortical bone these take the form of a drill-like group of osteoclasts boring a hole through the bone followed by osteoblasts that
close the resulting channel down to the dimensions of the normal
haversian canals. In trabecular remodelling the mechanism is
less clear but there is no shortage of evidence for its
existence.

The stimuli that control the bone turnover are discussed
below but it is important to stress that it is not a random
process and is in fact controlled by a complex regulatory
mechanism.

1.2.3 Bone Architecture

Two different formations of bone are found and these are
known as woven and lamellar bone. The former is usually only a
transient phase found during rapid growth or in the early stages
of fracture repair and is just a loose framework of trabeculae
that, as the name suggests, resembles woven cloth. This weak
formation is normally replaced by the stronger lamellar bone.
The infantile disease fragilitas ossium is an example of this
transition failing to happen.

Lamellar bone is made of layers of bone tissue, with
successive layers having different collagen alignments, building
up a structure similar to plywood. Two macroscopic forms of
lamellar bone are found and are known as cortical and trabecular
bone.
Fig. 1.2 Diagram of cortical and trabecular bone.  
(From Hahn, Hospital Practice, 21(1986)73-79)
1.2.3.1 Cortical Bone

Cortical, or compact bone forms the shafts of the long bones and also the outer shell of the irregular and flat bones. It is made up of rod-like units called Haversian canals or osteones. These are channels that contain the nerves and blood vessels and are surrounded by lamellae, up to 14 in number, with typical diameters for these canals being 0.2-0.5mm. These osteones branch and interweave through the bone but with the long axis tending to follow lines of stress.

1.2.3.2 Trabecular Bone

This is also known as cancellous bone or spongiosa and is found at the expanded ends of the long bones and within the irregular bones. It is made of strands of lamellar bone, called trabeculae, that mesh together in a pattern initially dictated by genetic information but subsequently remodelled by the stress patterns within the bone. The surfaces of the cancellous bone are covered in a layer of bone cells, including undifferentiated mesenchymal lining cells. Due to its spongy structure the trabecular bone has a much greater effective area than the cortical bone and therefore has more cells per unit volume. This leads to a greater metabolic activity in the spongiosa, in general, than in compact bone making the former more responsive to stimuli.

The interstices in spongiosa are filled with bone marrow
which may be haematogenous (red) marrow or the fatty (yellow) variety, depending on age and the skeletal location. In adults red marrow is only found in the axial skeleton and in the upper parts of the humerus and femur whereas in children it is found throughout the body (CRI-81).

1.3 Bone Metabolism

Bone is a living tissue despite its rigid nature and is involved in the body’s metabolic processes. In the young the bones are obviously undergoing changes as they are growing in size and cartilage is being turned into hard bone. Adult bone does not undergo such profound alterations and its primary biochemical activity is connected with calcium homeostasis.

The body is continually losing calcium in faeces, urine and, in the case of pregnancy, to the foetus and to breast milk. If absorption from the intestine is not able to replenish this loss then bone is resorbed, releasing calcium ions to the plasma in order to maintain constant levels of blood calcium.

1.3.1 Calcium Regulating Hormones

Of the calcium circulating in the body fluids only about 47% is carried as free ions, the remainder being in a bound form, but it is this ionic calcium that controls the primary calcium regulators and also mediates the effect of some of the bone regulating hormones. High levels of calcium in the extra-cellular

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Bone-Resorbing Stimulus

Bone Matrix

Osteoblast

Collagenase

Coupling Signal

Mononuclear Osteoclast Precursors

Osteoclast

Bone-Forming Stimulus

Insulin, IGF-I, Other Growth Factors, Physical Stimuli?

Osteoblast Precursors

Coupling Signals?

Osteoclast

Lining Cells

Mineralized Bone

New Bone

Canaliculi

Lining Cells

Osteocyte

Fig. 1.3 Outline of bone remodelling.
(From Hahn, Hospital Practice 21(1986)73-79)
fluid will, of course, encourage bone mineralisation. The role of the phosphate ion in bone metabolism is not clearly understood but may be at least as important as the calcium and undergoes much greater physiological variation in concentration, low levels invariably giving rise to osteomalacia.

1.3.1.1 Parathyroid Hormone

When calcium levels fall the release of parathyroid hormone (PTH) rapidly increases. Its influence on the gut, mediated by vitamin D, is to increase active calcium absorption and it also increases calcium reabsorption in the kidney. PTH has a very powerful effect on bone cells causing a fall in osteoblastic activity, thus reducing collagen production, and it makes them pull away from the bone surface, allowing free access for the osteoclasts. The bone resorbing cells themselves have no PTH receptors but are stimulated to increase bone removal by some signal from the osteoblast. This increase in resorption and decrease in formation of bone will lead to a rise in the circulating calcium levels.

1.3.1.2 Calcitonin

This hormone is produced in the thyroid in response to hypercalcaemia. Its actions are to reduce renal reabsorption of electrolytes, including calcium, and to directly reduce osteoclast activity. At normal physiological levels it appears to have little influence but when present in pharmacological
Fig. 1.4 Calcium Homeostasis.
(From Smith, 1979, "Biochemical Disorders of the Skeleton", Butterworths, London)

Fig. 1.5 Age dependence of 3rd metacarpal measured in standardized aluminium equivalent.
(From Aitken, 1984, "Osteoporosis", Wiley, Bristol)
levels it causes a very rapid reduction in bone resorption. Its production can also be stimulated by gastrin and it is thought that the intestine may be the primary stimulator of this hormone.

1.3.1.3 Vitamin D

Despite its name it is perhaps more accurate to consider vitamin D as a being a hormone. In the form absorbed through the small intestine (from food such as fish and dairy products) or manufactured in the skin by the action of sunlight it is not metabolically active. It first of all undergoes hydroxylation in the liver to form 25(OH)D which then circulates in high levels in the serum, the exact amount depending on vitamin D intake. The active metabolite, 1,25(OH)$_2$D is then formed from this circulating pool of 25(OH)D in the mitochondria of the kidneys under the action of an hydroxylase. The precise factors controlling this production have not all been identified but it is known that increased levels of PTH (related to hypocalcaemia) and low phosphate levels both increase the rate of hydroxylation. The effect of 1,25(OH)$_2$D on the gut is to increase the active absorption of calcium and phosphate hence a dietary deficiency of vitamin D in children leads to rickets, a disease characterised by poor mineralisation of bone tissue. 1,25(OH)$_2$D also directly suppresses the osteoblasts and stimulates osteoclastic resorption, hence reducing bone mass.
1.3.2 Other Factors

The bone cells respond to hormones other than the calcium regulators. In particular cortisol and other glucocorticoids, which are necessary for osteoblast differentiation, can decrease their activity if present in high levels. Simultaneously calcium absorption from the gut is reduced which, via PTH, leads to an increase in osteoclastic resorption.

Whilst the bone cells have no receptors for sex hormones they are affected indirectly by both androgens and oestrogens. Testosterone has an anabolic influence on bone, possibly due to increased muscle and hence higher stresses to stimulate formation. Oestrogen causes an increase in bone turnover and reduces the osteoclasts' sensitivity to PTH and other stimuli. The reduction in oestrogen at the female menopause therefore leads to an increase in bone loss.

As has already been mentioned, stress applied to a bone either through weight bearing or by muscle tension will stimulate the osteoblasts and lead to an increase in bone tissue. The reason why this should happen is not known but it has been suggested that a piezo-electric effect in the hydroxyapatite crystal may be responsible.
1.4 Osteopenia

There are, of course, many diseases associated with the skeleton but the ones of interest to this work are those characterised by a deficiency in bone mass, when compared to the normal values for age, sex and race. This class of disorders is given the general name of osteopenia, with the different forms of bone loss being classified as osteomalacia, osteitis fibrosa and osteoporosis.

1.4.1 Osteomalacia

Osteomalacia is diagnosed when there is insufficient mineralisation of the osteoid. The best known form is rickets found as a result of vitamin D deficiency. Without the action of $1,25(\text{OH})_2\text{D}$ to cause the active absorption of calcium and phosphate from the gut the body is unable to provide sufficient of these ions for collagenic calcification. Various forms of defective vitamin D metabolism, such as insufficient renal hydroxylation can also lead to osteomalacia and is known as pseudo-vitamin D deficiency rickets. Excessive use of ant-acids such as aluminium or magnesium hydroxide can also lead to osteomalacia as these bind up phosphate ions hence causing hypophosphataemia.

1.4.2 Osteitis Fibrosa

Osteitis fibrosa is the result of resorbed bone being
replaced by fibrous tissue rather than fresh osteoid. This can be caused by the increased levels of PTH found in cases of hyperparathyroidism. With the heightened amount of PTH osteoclastic resorption is accelerated to such rates that the osteoblasts are no longer able to keep up. Renal failure can also lead to this condition, with associated osteomalacia, as phosphate retention and decreasing levels of $1,25(OH)_2D$ give rise to high PTH levels. A further complication in the case of kidney disease is the possibility of aluminium from dialysis fluids being retained in the bones and eventually poisoning the osteoblasts.

1.4.3 Osteoporosis

In osteoporosis, unlike the above disorders, there is nothing histologically wrong with the bone i.e. there is normal mineralisation of collagen, but it is found that the total quantity of bone tissue in a given volume has decreased being replaced by marrow. This reduction in bone mass is found to occur naturally with increasing age but other factors can accelerate this process leading to a marked increase in bone fragility. The best known of these is the female menopause. A number of books and reviews have been written on this subject and a few are given in the bibliography at the end of this chapter.

There is some discrepancy as to what the true definition of osteoporosis actually is. Aitken for instance describes
osteoporosis as "a quantitative loss of bone substance sufficient to render the affected part or parts of the skeleton abnormally susceptible to mechanical failure" (AIT 84), but Smith suggests that osteoporosis should only refer to bone that has undergone structural failure (SMI 79b). The former definition has been used for this discussion as in many cases the difference between a fractured and a non-fractured osteoporotic bone is only a minor trauma.

It is usual (e.g. HAH 86) to use the term secondary osteoporosis when a medical cause for the bone loss is apparent and to describe those cases without an obvious cause as primary, postmenopausal or involutional osteoporosis. Some authors (AIT 84, RIG 86), however suggest that such a distinction is unhelpful and that the syndrome should be considered as a multifactorial problem with some causes, such as age, always having an influence but some other risk factor perhaps being the primary reason in a given case. In the interests of clarity a distinction between primary and secondary osteoporosis will be made in the following sections but this is not to deny the many-faceted nature of the disorder.

1.4.3.1 Primary, Postmenopausal and Involutional Osteoporosis

The age dependence of bone mass is illustrated in Fig. 1.5. This clearly shows the increase in bone tissue, by radial and longitudinal growth, until about age 30, and then a steady decrease with age. In advanced old age a woman may have lost 35%
of her cortical bone and 50% of her spongiosa. For a man the loss will only be about two thirds as great. The loss of compact bone starts at about 40 years old with an initial rate of 0.3–0.5% per year that increases with age and then slows and stops in later life. Such a pattern is harder to define in the case of trabecular loss, perhaps due to different sites altering at varying rates and at different times, but it would appear to commence a decade earlier than the cortical decrease.

Women experience a second, menopausal pattern of bone loss superimposed on the age dependent trend. Immediately after menopause the resorption rate for cortical bone may be 2–3% per year, decreasing to the normal, age-related loss rate in about 8 to 10 years. The associated reduction in trabecular bone seems to be at an even greater rate but with a shorter duration.

These losses in osseous tissue increase the fragility of the bones and hence cause a rise in fracture incidence with advancing age. This increase is also partly due to the greater likelihood of trauma in the elderly, caused by deteriorating eyesight and co-ordination and the influence of some drug treatments often given to old people (AIT 84). Not all fractures in osteoporotics are, however, caused by major trauma: some can be the result of very minimal stress or may even apparently occur spontaneously for extremely fragile bone.

The incidence of Colles’ (distal forearm) and vertebral fractures increases in the first few years post-menopause, these
being sites of mainly trabecular bone. In later life the probability of fractures in sites of mixed trabecular and compact bone, such as the hip, pelvis and proximal humerus and tibia is found to rise. It should be noted that fractures of the long bones i.e. sites of pure cortical bone, are not found to be dependent on osteoporosis.

The reason for the loss of bone mass lies with the regulatory mechanism that controls bone turnover. In young people resorption and formation are tightly coupled ensuring that the bone mass stays constant, but from about age 30 the action of the remodelling units gives a net loss in bone tissue. Many factors are believed to be involved in this failure of the calcium regulators. From about the age of 70 calcium absorption from the gut decreases, possibly due to the associated drop in vitamin D hydroxylation in the kidneys. An increase in PTH is also found at about this age, possibly triggered by the fall in blood calcium.

In the case of the female, postmenopausal loss the fall in oestrogen levels is believed to cause an increase in resorption. Study of the natural menopause is difficult as the changes in sex hormones are variable and gradual. It is found that oopherectomy, however, is often followed by severe bone loss that can be slowed or stopped by oestrogen supplements and a form of hypogonadism not uncommon in female long distance runners leads to a fall in vertebral bone density. A clear relationship between oestrogen deficiency and bone loss seems to
indicated by this evidence.

Another factor that makes women more susceptible to the problems of osteoporosis is the smaller initial size of their bones compared to men's making them less able to withstand a reduction in osseous tissue (SMI 87a). The fracture incidence in black women, who tend to have larger bones, is less than that in the European or Asian races (RIG 86).

Various dietary deficiencies may also play a role in osteoporosis. Clearly insufficient calcium or phosphate intake will lead to bone resorption and vitamin C is necessary for collagen production. Whilst calcium deficiency is uncommon, people with lactase deficiency, who thus eat few dairy products, have an increased incidence of osteoporosis.

As has already been indicated stress tends to encourage bone formation and so weight bearing exercise will strengthen bones. Conversely immobilisation will cause bone resorption and thus lead to osteoporosis in those parts of the skeleton that are not being used.

Other behavioural influences include smoking and excessive alcohol consumption, both of which are considered to be risk factors: the latter directly supressing osteoblast activity.

Some authors (e.g. RIG 86, SMI 79b) consider primary osteoporosis as two distinct syndromes: postmenopausal and senile
osteoporosis. The former is predominantly a female disorder (though a few hypogonadic men also suffer from it) and is characterised by an excessive rate of trabecular bone loss, up to three times the normal in some cases. This in turn leads to an increase in crushed vertebrae and Colles’ fractures. The cause of this accelerated loss is apparently due to impaired 1,25(OH)₂D metabolism though PTH levels are lower, and calcitonin levels higher than normal. Low levels of oestrogen are believed to be the cause but there has to be some contributory factor as not all postmenopausal women suffer despite all having uniformly low levels of sex hormone.

Senile osteoporosis is found in both sexes, but women still having a higher incidence, presumably due to their lower initial bone mass. This form is the result of the natural age-dependent loss reducing the bones to a dangerously low level. The sort of fractures associated with this syndrome are those of the hip and also vertebral wedging. Reduced osteoblast function caused by impaired 1,25(OH)₂D metabolism and the associated hypocalcaemia and PTH increase are thought to be the mechanism responsible.

1.4.3.2 Secondary Osteoporosis

Various medical disorders will lead to osteoporosis, those of major interest are:

1. Corticosteroid excess, either naturally as in Cushing’s
syndrome, or artificially as in the case of transplant patients where it is used to inhibit the body's rejection mechanisms, will suppress calcium absorption and thus lead to bone being broken down to maintain calcium levels.

2. Hypogonadism in both sexes leads to bone loss but the mechanism responsible is not clear, especially in the male.

3. Hyperthyroidism increases osteoclastic resorption due to higher levels of thyroid hormone. It is a greater problem in the young as the turnover rate of the bone is higher.

1.4.3.3 Treatment of Osteoporosis

The usual treatments given to osteoporotic patients are dietary calcium supplements and oestrogen and calcitonin hormonal replacements. These only suppress bone resorption and do not directly stimulate bone formation. There are also problems associated with their administration. Oestrogen has to be given with progestin to avoid an increase in cancer risk and is also found to lead to thrombosis in some cases, perhaps due to the usual (oral) method of taking the hormone subjecting the liver to excessive levels. Calcitonin cannot be taken orally and has to be injected, though some work has been done recently on the use of a nasal spray (RIG 86, RUE 87). In order to try to stimulate bone formation sodium fluoride is sometimes given but its toxicity can cause gastric problems.
Clearly prevention is better than cure and hormone replacement therapy (HRT) at the menopause i.e. artificially replenishing the lost oestrogen may significantly reduce the likelihood of osteoporosis. The problems associated with taking oestrogen and the costs involved, however, indicate that HRT should only be considered for those most at risk. Defining such a group of likely sufferers is not easy, though historical risk factors, e.g. race, age at menopause and family history of osteoporosis may help (RIG-86), actual bone measurements seem to be the best indicators of probable fracture victims (WAS 87, BUC 87).
Bibliography for Chapter 1

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2.1 Introduction

A number of techniques have been proposed for measuring bone "mass" or "density" and for a review the reader may like to consider Cohn's work (COH 81) or the more recent book by Avioli (AVI 83).

The purposes in trying to ascertain the bone status can be considered as basically twofold:

1) To identify individuals with lower than normal amounts of bone tissue i.e. the fracture risk group.

2) To monitor changes in the bone and thus perhaps to monitor the progress of treatment being administered.

While these aims are generally true for all osteopenic disorders the problem of major clinical interest is osteoporosis and especially how to isolate those members of the female population most at risk (RIG 86).

Some of the more traditional techniques for studying bone and calcium metabolism such as bone biopsy (histomorphometry) and calcium balance (monitoring calcium intake and excretion) are very demanding on the analysis laboratory in terms of the tests required, and on the patient due to physical discomfort or plain inconvenience. It could be said that the ideal method
should fulfill the following criteria:

1) Easy and straightforward to apply.
2) Non-invasive.
3) Accurate and precise.
4) Good predictive power.
5) Low radiation dose.
6) Inexpensive: in both capital investment and running costs.

2.2 Radiography

A radiograph of a skeletal site is a cheap, straightforward method of examination and gives only a low dose, approximately 400 uSv to the region of interest (AIT 84). The analysis of the radiograph, however, may be done in different ways: either qualitatively or by some quantitative means such as radiogrammetry or photodensitometry.

2.2.1 Qualitative Morphometry

This is a qualitative study of the number and patterns of the trabeculae in the spongiosa and is usually carried out on radiographs of the spine or the femoral head. In both cases a subjective scale is used to grade the bones from healthy to very fragile. A strong vertebra, for instance, will be uniformly opaque but with the onset of osteoporosis the horizontal trabeculae will be preferentially resorbed to leave the load bearing vertical ones clearly visible on a radiograph. In an
extreme case a vertebra will appear translucent (AIT 84, EVA 87). When examining the neck of the femur the Singh index is the system normally employed to grade the stress-related patterns of the bone strands (AIT 84).

The usefulness of these techniques is much debated (MAZ 83b) but in the hands of an experienced user good results are obtainable and the method is still very much in use (McL 87). Nonetheless it is obviously a subjective grading that is applied and so the values given by this technique have limited objectivity and it would, perhaps, be unwise to treat them as an absolute measure of the skeletal status.

2.2.2 Radiogrammetry

The measurement of cortical bone thickness and bone width, usually of the metacarpals (hand) yields parameters such as "percentage cortical thickness" (JOH 83, AIT 84) which have proved to be useful in studying skeletal disorders (MEE 81) but once again a degree of subjectivity is involved in the measurement procedure. Modern developments of this technique involve the use of magnified radiographs to look at the microscopic structure of the bone (MEE 87).

2.2.3 Photodensitometry and Digital Radiography

This relies on the opacity of the image on an X-ray film being dependent on the amount of bone tissue present. The usual
method is to take a radiograph, again often of the hand, along with a calibration phantom such as an aluminium or hydroxyapatite wedge to overcome variabilities in the X-ray tube output and film development processes (COL 81). A light densitometer or a digitisation process can be used to compare the bone image to the phantom and thus quantify the amount of bone present. There are problems, however, with scattering and beam hardening and also non-uniformities in the beam and film response across the image. There is also the overlying soft tissue that contributes to the beam attenuation, but this can be partly accounted for by using a water bath to give an effectively uniform thickness of tissue or tissue equivalent material. With the ready availability of computer power a digitised image can be easily processed and comparisons made with previous radiographs; Zeichner (ZEI 87), for instance, has reported detecting localised changes of only 0.3% using such a technique.

2.3 Single and Dual Photon Absorptiometry

This uses a collimated gamma-ray beam and detector to measure the attenuation of bone tissue as in quantitative radiography. It was first demonstrated by Cameron and Sorenson (CAM 63) using an $^{125}$I source as a means of overcoming the problems of non-uniformity and of reducing beam hardening and scattering in the latter method. If a mono-energetic source is used then there is no beam hardening at all.
A schematic diagram of the apparatus used is given in Fig. 2.1, showing how the beam is scanned across the region of interest. It is necessary for the length of the attenuating tissue to be constant and so shaped pieces of tissue equivalent material or a water bath must be used. Assuming a simple two component model as shown in Fig. 2.2 it can be seen that the transmitted intensity through soft tissue, \( I' \), and that through bone and soft tissue, \( I \), will be given by:

\[
\begin{align*}
I' &= I_0 \exp(-u_tT) \\
I &= I_0 \exp(-u_tT_b - u_bT_t)
\end{align*}
\]  

(2.1)

Where \( u_{b,t} \) are the photon linear attenuation coefficients for bone and tissue respectively and \( T_{b,t} \) are the respective thicknesses, with \( T \) being the total thickness. It follows that:

\[
T_b = \ln(I'/I)/(u_b - u_t)
\]  

(2.2)

By assuming values for \( u_b \) and \( u_t \) it is possible to estimate the equivalent thickness of bone present, and by measuring closely spaced values of \( T_b \) to find the effective cross-sectional area. This value may be multiplied by the density of bone to give a figure with units of Kg / m which is often called the "bone mineral content". This is clearly different to the more common definition of bone mineral content as mass per unit volume.

The isotopic sources most often used in these machines
are $^{125}$I and $^{241}$Am. The former has a rather short half life (60 days) but is less sensitive to changes in fat content, due to its lower photon energy (27 KeV), compared to the latter (60 Kev) (MAZ 81).

The use of single or closely spaced energies (e.g. $^{125}$I) limits single photon absorptiometry (SPA) to the analysis of distal sites only, such as the radius, os calcis (heel) or hand. It has however proved to be precise and to give a low dose, Nicholl reporting 1.9% precision for a dose of only 6 uGy for his study of the hand (NIC 87b).

In order to examine axial skeletal sites dual photon absorptiometry (DPA) is used, enabling the restriction on uniform thickness to be lifted. Considering equation (2.1) for two gamma-ray energies denoted by subscripts 1 and 2 we have:

$$I_1' = I_{01} \exp(-u_{1T}t - u_{1b}T_b)$$
$$I_2' = I_{02} \exp(-u_{2T}t - u_{2b}T_b)$$

which yields (TOT 83):

$$T_b = \frac{u_{2t} \ln(I_{01}/I_1') - u_{1t} \ln(I_{02}/I_2')}{u_{2t}u_{1b} - u_{1t}u_{2b}}$$

(2.4)

This is usually related to a baseline defined by the adjacent soft tissues. Note that this analysis assumes a two phase model and hence that the fat distribution is uniform.
throughout all the soft tissues including the bone marrow. As measurements are made for two energies and the results combined the statistical precision of DPA is less than that of SPA for a given dose. It can, however, be applied to any skeletal site including the spine and femoral neck (MAZ 83b) and can also be used to estimate total body calcium (MAZ 84).

The majority of commercially available DPA machines use $^{153}$Gd (44 KeV and 100 KeV, half life 242 days) sources with the most modern ones achieving 0.7% precision in measurements of the spine for a dose of 70 uSV (NIE 87). Studies have been made on the feasibility of using longer lived, cheaper sources: e.g. Smith et al (SMI 83) and Armes et al (ARM 87) have looked at a combination of $^{241}$Am and $^{137}$Cs (60 KeV and 662 KeV) and the former achieved a statistical precision of order 1% for 150 uSv dose. Recently machines have been developed that use a rapidly switching X-ray tube instead of an isotopic source. The higher flux available enables faster scan times (5 minutes compared with 30 minutes for conventional DPA) and a narrow collimation, yielding a better image and a lower overall dose. Mazess (MAZ 87) and Sartoris (SAR 87) both quote 0.5% precisions for a dose of only 20 uSv for their rival machines.

There are problems associated with both SPA and DPA when it comes to inhomogeities in fat distribution. Adipose tissue has a lower linear attenuation coefficient than muscle and other soft tissues and hence any variabilities in its distribution will invalidate the two phase model essential to estimate the bone
content. Another difficulty is how to correct the values obtained for body size as the larger the person the more bone will be present and the skeleton strong enough for a 50 Kg woman would probably be inadequate for an 80 Kg man (MAZ 81, AIT 84). One technique tried has been to normalise the bone mineral content for the bone width but this has been shown to be questionable as it assumes a cylindrical shape for the bone (RUF 84). In a true clinical environment the precisions attainable seem to be poorer than those obtained with research machines, LeBlanc et al (LEB 86), for instance, report DPA only being sensitive to a change of order 5% in bone content.

Both SPA and DPA sum together all bone mineral along the beam path and do not discriminate between the compact and trabecular bone. This would, in principle, make the techniques less sensitive to changes in bone status than a method that is able to assess the more metabolically active spongiosa alone. It has been suggested by Mazess that as bone strength will depend on the cortex as well as the trabeculae DPA may be the best way of determining possible fracture risk (MAZ 83b). Certainly DPA and, to a lesser extent, SPA have achieved a good level of popularity and have been used for many clinical studies (e.g. HUT 87, MAZ 84, GEU 86).

2.4 In-Vivo Neutron Activation Analysis

The principle of neutron activation analysis (NAA) is to produce neutron rich isotopes of the elements of interest and to
detect the characteristic gamma-rays produced by their disintegrations. Using a suitably calibrated system it is thus possible to assess the amount of a given element or elements present. The source of neutrons may be a reactor, neutron generator, cyclotron, isotopic source (e.g. $^{241}$Am/Be) or a fission radionuclide such as $^{252}$Cf. When applied in-vivo, whole or part body irradiations can be done to ascertain the quantities of various elements, including calcium, present. For further information on in-vivo NAA in general the review of Chettle and Fremlin may be consulted (CHE 84) whereas for bone mass in particular Cohn’s book provides a useful overview (COH 81).

When studying bone tissue it is calcium content that is usually of primary concern though other elements such as sodium and chlorine (e.g. NIC 87a) and, of course, phosphorus (COH 78) can be monitored at the same time. The nuclear reaction normally used is (COH 81):

\[ ^{48}\text{Ca}(n,\gamma)^{49}\text{Ca} \rightarrow ^{49}\text{Sc} + e + 3.1\text{ MeV} \]  (2.5)

where $^{49}$Ca has a half life of 8.9 minutes, and so photon counting is done after an initial neutron irradiation. Unfortunately $^{48}$Ca has an abundance of only 0.185% and so the statistical precision is limited. Further complications that have to be considered are the inhomogeneities in both initial neutron flux and emitted gamma-rays. Despite these difficulties in-vivo NAA can achieve a precision of better than 3% in calcium measurements. The dose delivered, however, can be significant
with local activation of the forearm or hand giving 100 to 150 mSv (SMI 79a, EBI 86) and whole body NAA giving 10 mSv (NIC 87).

An alternative whole body NAA technique has been developed using the prompt gamma-rays generated by activation of the naturally abundant (97.0%) $^{40}$Ca (RYD 87):

$$^{40}\text{Ca}(n,\gamma)^{41}\text{Ca}$$  \hspace{1cm} (2.6)

The precision quoted for this method is 3% for a 5 mSv dose.

Another neutron based method of assessing the calcium levels present in-vivo relies on measuring the exhaled argon resulting from the reaction $^{40}\text{Ca}(n,\alpha)^{37}\text{Ar}$ but this technique does not appear to be as widespread as the delayed gamma counting one (CHE 84).

Work has also been done looking not just at calcium levels but at the ratio of calcium to phosphorus (COH 78, CHE 84).

Though NAA is capable of reasonable precision in estimating calcium levels the dose delivered prohibits its use as a means for cross-sectional screening programmes or for longitudinal studies on patients. Its role is much more as a research tool than as a routine, clinical method of studying bone status.
2.5 Ultrasound

The application of ultrasound technology to the problems of bone mass is an attractive one as there are no associated dose risks, as far as is known. One technique explored was the measurement of ultrasound velocity in bone to deduce the modulus of elasticity (GRE 81) but this only seemed to have any discriminatory ability when combined with measurements of bone mineral content as found by using SPA.

A method that has produced interesting results is that of measuring the broadband ultrasound attenuation (BUA) through the os calcis (heel bone), a quantity found for only a one second scan time. The magnitude and frequency dependence of this attenuation would appear to be dependent on the amount of bone present and also its structure (LAN 84). It is worth noting, however, that the underlying physics is at present poorly understood. Comparisons of the technique with SPA show a good correlation but with BUA having a poorer precision (POL 86). Currently variability is of the order of 3% (PET 87) but the technique is new and if further improvements are possible it may become the favoured method for bone mineral measurements. To do this it will have to prove its ability to diagnose fracture risk with a reasonable degree of accuracy and while preliminary results are encouraging it is not possible at present to assess BUA’s predictive power.
2.6 Computerised Tomography

X-ray computerised tomography (CT) has become an established technique in medicine for non-invasive imaging and is gaining acceptance as a general method of non-destructive testing. A detailed explanation would be out of place in this discussion: rather the works of Brooks and Di Chiro (BRO 76); Kouris, Spyrou and Jackson (KOU 82) and Webb (WEB 87a) should be consulted for thorough reviews of the theory and practical implementation of CT. The basic principle is that a set of X-ray transmission measurements, taken at different orientations through the body can be mathematically reconstructed to give a two-dimensional map or image of the linear attenuation. These linear attenuation coefficients are normally quoted in terms of Hounsfield numbers (KOU 82): a scale defined such that water has a value of 0 and air -1000.

If one considers the Hounsfield numbers in the image that correspond to skeletal sites then they will be dependent on the quantity of bone present in the same manner as in SPA and DPA. There is the added advantage of being able to see the bone in cross section and to study the spongiosa independently of the cortex.

2.6.1 X-ray Transmission Tomography

In practice the use of an X-ray tomography image to provide accurate, quantitative data relating to bone tissue is
not straight forward due to polychromaticity of the X-ray source (leading to beam hardening i.e. greater absorption for the lower energy components of the spectrum), detector and source variations and radiation scatter. Modern CT scanners are usually designed for maximum image quality and speed of acquisition at the expense of ensuring system linearity (PUL 86). In an effort to overcome these problems Cann and Genant (CAN 80) placed a specially made calibration phantom, containing solutions of potassium hydrogen orthophosphate ($K_2HPO_4$ - a bone equivalent material), under the patient being scanned. This enabled a direct calibration of the trabecular bone to be made by comparison with the solutions in the phantom, the bone mass being expressed as a $K_2HPO_4$ concentration (mg/ml). The assumption made is that the variabilities in Hounsfield number due to the above effects will be constant across the image so that the change in the values for the phantom will be the same as for bone tissue. Though this may not be totally valid a long term precision of 2.8% was achieved for an vertebral phantom (CAN 80).

The technique has proved very popular as a means of measuring the trabecular bone of the spine with many centres carrying out population studies to estimate normal values and biological variation on several continents (e.g. BER 87, MON 87 FUJ 87). The work of Banks and Stevenson (BAN 86), for example, using a standard CT machine, produced in-vivo precisions of 2.2% for a surface dose of 16 mGy enabling them to make a study on the progress of patients undergoing hormone replacement therapy. Not all studies have been limited to the vertebrae: e.g.
Sartoris et al (SAR 86) used CT to examine the femoral head.

Recent developments in this method include the use of sophisticated software to give reproducible regions of interest in the image (WAN 87, GRA 87) and also to analyse the texture of the trabecular pattern (KLI 87). This latter idea is an interesting one as, of course, the strength of the bone is very much dependent on the arrangement of the trabeculae and not just the quantity of osseous tissue. After a number of years of widespread use the Cann and Genant phantom may soon be replaced as the standard for calibration by new phantoms made of hydroxyapatite suspended in a water equivalent plastic currently being developed by Siemens (KAL 87) and by General Electric (LON 87).

There is still some debate as to the optimum choice for the region of interest (ROI) within the image of a vertebra. At present the choice is largely dictated by the software used for the image analysis. The favoured approach would appear to be that of Bank's (BAN 87) where the largest possible area within the trabecular bone is used.

A more serious problem to be overcome, however, is the influence of fluctuations in bone marrow composition on the Hounsfield numbers measured. A low level of bone tissue in red marrow will appear identical to a greater quantity embedded in yellow (i.e. fatty) marrow. Mazess (MAZ 83a) has estimated an error of 36 Kg m\(^{-3}\) (3-4%) in the density of bone may result from
this fat variability, though Webber (WEB 87b) in his review of the effects of fat on bone density measurements suggests a figure only of 5 Kg m$^{-3}$ (0.5%) based on more accurate values for the density of yellow marrow.

2.6.2 Dual-Energy X-ray Transmission Tomography

This problem of fat dependence has led to several investigations in the use of dual-energy CT to quantify bone mass. It has been shown by Jackson and Hawkes (HAW 80, JAC 83) that for the photon energies and range of atomic numbers encountered in radiology the mass attenuation coefficient (u/p) of a tissue, at energy E, can be represented as the weighted sum of the coefficients for two reference materials, 1 and 2:

$$u(E)/p = a_1(u_1(E)/p_1) + a_2(u_2(E)/p_2)$$  \hspace{1cm} (2.7)

where $a_1$ and $a_2$ may take negative values. If one of the materials is water, designated by the subscript w, in association with a reference material, r, then 2.7 becomes:

$$u(E) = p_w(m_wu_w(E)/p_w + m_ru_r(E)/p_r)$$  \hspace{1cm} (2.8)

where:

$$m_w = a_wp_w/p_w; \hspace{1cm} m_r = a_rp_r/p_r$$  \hspace{1cm} (2.9)

$p = \text{tissue density}$
When this analysis is applied to a CT scanner with its polychromatic X-ray beams and using the Hounsfield scale it can be shown (HAW 86):

\[
\frac{H_m - H_w}{H_w - H_a} = m_w - 1 + m_r \frac{<u_r/p_r>}{<u_w/p_w>} \tag{2.10}
\]

where:

- \( H_m \) = Hounsfield number for a given energy
- \( H_w \) = Hounsfield number measured for water
- \( H_a \) = Hounsfield number measured for air
- \(<u/p> = \int (S(E)u(E)/p)dE / \int S(E)dE \) \tag{2.11}
- \( S(E) \) = energy spectrum of X-ray tube

By scanning water, air and a sample of the reference material at two tube voltages the last term in equation 2.10 for the two different spectra can be determined. Thus a scan of an unknown material at two different KVP settings will yield two simultaneous equations which can be solved for the coefficients \( m_w \) and \( m_r \), enabling tissue characterisation. If the reference material is a suitable bone equivalent, e.g. calcium chloride as used by Hawkes (HAW 86), then the value \( m_r \) will be a more accurate prediction of the bone mineral content than the estimate gained from a single energy measurement. In principle the bone could be characterised as water plus any chosen reference material but obviously it is more useful to have the "basis set" chosen as close as possible to the real tissues being analysed (BUR 87).
This method of reference material calibration has been used by Hawkes et al to characterise several tissues including bone (HAW 86). A number of studies of dual energy CT have, however, used a different technique based on the assumption of a common energy dependence for the separate components of the attenuation coefficients, an approximation that has been demonstrated to have a limited validity (JAC 83).

The application of dual-energy CT to bone densitometry has shown that it is more accurate than single energy CT (ADA 82, LAV 84, LAV 86), though the precision is, of course, lower and a higher dose given (BAN 86). Burgess, for example, found that for excised vertebrae, that were scanned and then analysed chemically to find their mineral content, the accuracy for single energy was limited to about 14 Kg m$^{-3}$ compared with 10 Kg m$^{-3}$ for dual-energy CT.

If ordinary CT machines are used for dual-energy analysis then it is necessary to make two separate scans at different tube voltages and this inevitably leads to errors due to patient movement (ADA 82, DUN 84). To overcome this problem a rapid-switching tube has been used enabling both sets of data to be acquired in one scan (KAL 86). Results from this machine again indicate that dual-energy CT gives improved accuracy as it is less sensitive to fat variability.

Dual-energy CT is still largely experimental and is only being used in a few centres, presumably limited by the high dose
2.6.3 Low Dose Gamma-ray Transmission Tomography

To produce cross-sectional images of the axial skeleton X-ray CT is needed but for appendicular sites it is possible to use a radionuclide as the photon source, greatly reducing the machine complexity and the dose delivered to the patient. In practice $^{125}$I is invariably used though recently in-vitro experiments have been conducted using other sources such as $^{153}$Gd (MOR 87).

The technique was originally developed by Ruegsegger (RUE 76) as a progression from ordinary SPA. Instead of taking a single linear scan across the distal radius, 48 such scans, or projections, were collected each at a different angle uniformly spaced through 180 degrees of rotation. This data was then reconstructed to form an image of a section through the bone. Thus the trabecular and cortical bone could be distinguished, unlike an SPA scan. The original machine had a precision of 2% for a dose of 50 uSv (RUE 76) but later models had a reported reproducibility of 0.3% (RUE 81) for the same dose and a few other centres have now built machines with comparable performance (e.g. HAN 82, HOS 85 & 86).

By using a lower photon energy than whole-body scanners (29 keV as opposed to approximately 70 keV) this method also suffers less from the problems of fat variability (HAN 82). The reason for this can be understood by considering Fig. 2.3 where
it can be seen that at the lower energy the attenuation coefficient for bone is much greater relative to that for soft tissues than at the usual X-ray energies hence reducing the influence of the marrow on the measured values.

Isotope based CT machines have not gained a high level of general acceptance and no commercial machines are thought to be available. Nonetheless the research models that do exist have been used in population studies to determine normal values (EXN 79), to monitor post-menopausal bone loss (RUE 84) and recently to monitor the progress of patients receiving calcitonin treatment (RUE 87).

2.7 Photon Scattering

The use of gamma-ray scattering has been investigated by several workers but has not achieved such widespread use as CT or DPA (AIR 87). A fairly detailed review of these techniques is, however, essential for the work to be presented in this thesis. To give an outline of the theory underlying the technique a brief summary of the interactions of gamma-rays with matter is also required.

2.7.1 Interactions of gamma-rays with matter

For the range of photon energies and atomic numbers encountered in diagnostic radiology there are three interactions to be considered: photoelectric absorption, incoherent
Fig. 2.3 Photon linear attenuation coefficients versus energy.
(From KOU 82)

Fig. 2.4
(Polar diagram of the differential cross section per electron for Compton scattering. Curves labeled according to $x = h\omega/mc^2$ of incident photon. Unit of $d\sigma/d\omega = 10^{-26}$ cm$^{-2}$ sr$^{-1}$.)
(From Segre, "Nuclei and Particles", 2nd Ed., Benjamin, New York, 1977)
scattering and coherent scattering. Other mechanisms such as nuclear Thomson scattering and Delbruck scattering (due to vacuum polarisation by the nucleus) are not significant and pair production cannot occur for photon energies below 1.022 MeV (i.e. two electron rest masses).

2.7.1.1 Photoelectric Absorption

In photoelectric absorption the photon is completely absorbed by an atom, the energy being transferred to an electron that is then ejected from the atom. It should be noted that this transfer cannot occur between a photon and a free electron as it is not then possible to conserve both energy and momentum. Calculations of the photoelectric cross-sections for atoms \( a \sigma^{\text{ph}} \) are quite complex (JAC 81), the simplest approach being the plane wave Born approximation which yields the much quoted form for low energies:

\[
a \sigma^{\text{ph}} \propto Z^5 E^{-3.5}
\]  

(2.12)

and for relativistic energies:

\[
a \sigma^{\text{ph}} \propto Z^5 E^{-1}
\]  

(2.13)

where \( E \) is the photon energy and \( Z \) is the atomic number. It must be stressed that these are not accurate but they do indicate the the dependence of the cross-section on energy and atomic number demonstrating how it increases for the lower energies and higher
2.7.1.2 Incoherent Scattering

When a photon "collides" with a free electron it will be deflected, i.e. scattered, and its new energy, $E_1$, will be given by:

$$E_1 = \frac{E_0}{1 + (E_0/mc^2)(1 - \cos \theta)} \tag{2.14}$$

where $E_0$ is the initial photon energy, $mc^2$ is the rest mass energy of an electron and $\theta$ is the scattering angle.

This formula was derived by Compton (COM 23) and was to play an important part in the development of the quantum theory.

The angular dependence for the scattered, unpolarised photons is given by the Klein-Nishina differential cross-section (JAC 81):

$$\frac{d\sigma^{KN}}{d\Omega} = \frac{1}{2mc^2} y^2 (1/y + y - \sin^2 \theta) \tag{2.15}$$

where:

$$y = 1/(1 + E(1 - \cos \theta)/mc^2) \tag{2.16}$$

For low energies (100 KeV and below) this is roughly isotropic but it becomes more forward peaked with increasing
photon energy (Fig. 2.4).

When we consider ordinary matter, however, the electrons will be in bound states and not free. The influence this has on the cross-section is normally found using the impulse approximation which assumes that the electron-photon interaction is the same for all the electrons independent of their state and that the effects of binding can be represented by a multiplicative incoherent scattering function \( S(q, Z) \), giving:

\[
d \sigma_{\text{incoh}} = d e^{\text{KN}} S(q, Z)
\]

(2.17)

where \( q \) is the momentum transfer \( 2E/(\hbar c) \sin(\theta/2) \).

This function suppresses the extreme forward angles of scattering leading to a lobed shaped cross-section as shown if Fig. 2.5. for the energies of interest. At the higher photon energies, such that the binding energy of the electrons becomes insignificant the electrons will be effectively free and \( S(q, Z) \) becomes equal to \( Z \), giving the atomic cross-section:

\[
d \sigma_{\text{incoh}} = d e^{\text{KN}} Z
\]

(2.18)

The terms incoherent, inelastic and Compton scattering are often used interchangeably. Strictly speaking Compton scattering refers to interactions with free, or effectively free
electrons only but for consistency with published work in the field the more general usage will be adopted.

2.7.1.3 Elastic Scattering

The term elastic scattering indicates that the gamma-ray does not lose energy. It is often used synonymously with the expression coherent scattering which means there is a fixed phase relationship between incident and scattered photons. Again the common practice will be followed and, henceforth, no such fine distinction will be made.

Classically a free electron in an electromagnetic field will oscillate at the field frequency absorbing and re-emitting energy, thus acting as a scatterer. The differential cross-section for this interaction is given by the Thomson cross-section:

\[ \frac{d\sigma^{\text{Th}}}{d\Omega} = \frac{1}{4\pi} \frac{(e^2)^2}{(\frac{mc^2}{\omega})^2} (1 + \cos\theta) \]  
\[ (2.19) \]

This can also be found as the low energy limit of the Klein-Nishina cross-section (Fig. 2.4) but in this classical form it has no energy dependence.

As before the electrons in matter have to be considered as being in bound states and not as free electrons. The elastic scattering from an atom is known as Rayleigh scattering and is
given in the form factor approximation as:

\[ \frac{d}{d\Omega} \sigma^{\text{coh}} = |F(q,Z)|^2 \frac{d}{d\Omega} \sigma^{\text{Th}} \]  \hspace{1cm} (2.20)

where \( F(q,Z) \) is the atomic form factor. As in the case of the incoherent scattering the assumption is made that all the electrons experience the same interaction allowing the factorisation of the cross-section into the free electron form multiplied by a factor to account for the binding in the atom. This is not rigorously valid and is especially dubious at absorption edges but nonetheless equation 2.20 has been used widely to calculate the Rayleigh cross-section, usually employing the tabulations of form factors published by Hubbell et al (HUB 75 & 79). Bradley and Ghose (BRA 84) have challenged the accuracy of the normal form factors \( F(q,Z) \), suggesting errors of up to 10% may arise from their use. Exact calculations of coherent scattering are, however, very time consuming even on large computers and so these authors have put forward the use of modified form factors \( G(q,Z) \) as a suitable compromise. As yet their suggestion has not been adopted and current work published still uses the traditional form factor approach (HAR 87).

The effect of the form factor on the shape of the cross-section is shown in Figs. 2.5 & 2.6. The scattering is very much restricted to the forward angles, this forward peaking becoming more pronounced for higher energies, and the total cross-section also decreases with increasing energy.
Angular dependence of coherent and Compton attenuation coefficients for 103-2 keV photons.

Fig. 2.5
(From KER 80)

Fig 2.6
At the very simplest level a Thomas-Fermi approximation yields the often quoted form for the cross-section:

\[ \frac{d \sigma^{\text{coh}}}{d \Omega} \propto \frac{d \sigma^{\text{Th}}}{d \Omega} Z^3 \]  

(2.21)

Though useful as a guide to the effect of atomic number on the cross-section it is not valid in general (BRA 84). The use of a $Z^n$ parameterisation reveals that $n$ has to be function of the momentum transfer (i.e. angle and energy) and also of $Z$ itself.

2.7.1.4 Attenuation Coefficients

The absorption and scattering of photons in passing through matter causes attenuation of a radiation beam. The total cross-section for removal of gamma- or X-rays through a material will be given by the sum of the cross-sections for the different interactions:

\[ a \sigma = a \sigma^{\text{ph}} + a \sigma^{\text{coh}} + a \sigma^{\text{incoh}} \]  

(2.22)

From this the linear attenuation coefficient ($u$) may be derived as:

\[ u = n a \sigma = \left( \frac{p}{A} \right) N_A a \sigma \]  

(2.23)

where $p$ is the materials density, $n$ is the number of atoms per
unit volume, \( A \) is its atomic weight and \( N_A \) is Avogadro's number. For a mixture of elements it is possible to apply the mixture rule:

\[
\frac{u}{p} = \sum w_i \left( \frac{u_i}{p_i} \right)
\]

(2.24)

where \( w_i \) is the proportion by weight of the \( i \)th element. This expression ignores any chemical effects and while generally accurate may be inappropriate near absorption edges (JAC 81).

An accurate parameterisation for the linear attenuation coefficient has been published by Jackson and Hawkes (JAC 81) allowing estimates to better than 1\% for energies and atomic numbers found in medical radiography.

### 2.7.2 Compton Scattering Bone Densitometry

The principle of Compton scattering densitometry relies on the number of photons scattered being proportional to the number of electrons present and thus dependent on the physical density. It is based on the assumption that the Compton differential cross-section being given by equation 2.18 as discussed above.

\[
\frac{d a \sigma^{\text{incoh}}}{d \Omega} = Z \frac{d e \sigma^{\text{KN}}}{d \Omega}
\]

(2.18)

For a photon beam of initial intensity \( I \) incident on a
material with atomic number Z the intensity of Compton scattered photons at an angle θ will be given by \( S(\theta) \), where:

\[
S(\theta) = I \, n \, V \, Z \, \frac{d \sigma^{KN}(\theta)}{d \Omega}
\]

where \( n \) is the number of atoms per unit volume, and \( V \) is the interaction volume \( V \). This can be written as:

\[
S(\theta) = I \, N_a \, p \, V \, Z \, \frac{d \sigma^{KN}(\theta)}{d \Omega}
\]

Assuming the ratio \( Z/A \) to be constant for the elements of interest we therefore obtain:

\[
S(\theta) = \text{constant} \times p
\]

In practice the incident and scattered beams will be attenuated, in the case of bone densitometry the examination site will be a region of trabecular bone and so a correction for the effect of overlying soft tissue and cortical bone has to be carried out. This is usually achieved by using a two source method: the primary source having a photon energy \( E_1 \) and the secondary one emitting gamma-rays of energy \( E_2 \) where \( E_2 \) is equal to the energy of the Compton scattered primary photons, as shown schematically in Fig. 2.7. A scattering measurement, \( S_1 \) is made using the primary source and detector 2, and then the apparatus
FIG. 2.7 COMPTON SCATTER TECHNIQUE
(COURTESY OF J. HOLLOWAY)
rotated through 180 degrees and a second measurement $S_2$ taken. The product of these will be (WEB 76):

$$S_1 S_2 \propto p^2 \exp\left(-\int_{a_1}^{a_1'} u_1(x) \, dx\right) \exp\left(-\int_{b_1}^{b_1'} u_2(x) \, dx\right)$$  \hspace{1cm} (2.28)

where $u_1$ and $u_2$ are the linear attenuation coefficients for the energies $E_1$ and $E_2$.

This simplifies to:

$$S_1 S_2 \propto p^2 \exp\left(-\int_{a}^{a'} u_1(x) \, dx\right) \exp\left(-\int_{b}^{b'} u_2(x) \, dx\right)$$  \hspace{1cm} (2.29)

Transmission measurements, $T_1$ and $T_2$, made along AA' and BB' will give:

$$T_1 T_2 \propto \exp\left(-\int_{a}^{a'} u_1(x) \, dx\right) \exp\left(-\int_{b}^{b'} u_2(x) \, dx\right)$$  \hspace{1cm} (2.30)

Hence the density will be given by:

$$p \propto \frac{S_1 S_2}{T_1 T_2}$$  \hspace{1cm} (2.31)

The proportionality constant can be found for a given experimental arrangement by using a density standard, usually water (WEB 76). A correction then has to be made to account for the slightly different mean values of $Z/A$ for water and bone as used in equation 2.26.
This technique was first applied to bone density measurements by Garnett et al (GAR 73) and by Clarke and Van Dyk (CLA 73) but these original systems used fairly high photon energies and thus delivered large radiation doses. Garnett’s system gave a dose of order 0.1 Sv and so could only be used for in-vitro studies on excised vertebrae. Lower energy sources were used by Karjalainen and Olkkonen (KAR 74, OLK 75) who employed $^{170}$Tm (87 KeV) and assumed the Compton energy shift to be sufficiently small to allow the same source to be used for the transmission measurements. They applied this one-source method to excised vertebrae but considered SPA to be more sensitive to changes in bone density.

Webber and Kennet (WEB 76) were the first to build a Compton densitometer suitable for in-vivo work and they have used it to examine the heel-bone (os calcis) of a number of volunteers. Their equipment used $^{153}$Sm (103 KeV) as the primary source and $^{170}$Tm (87 KeV) for the secondary one, with a scattering angle of 90 degrees. This combination gave a dose of 1.6 mSv for a measurement with an accuracy of 22 Kg m$^{-3}$.

The various sources of error encountered in the use of this apparatus were investigated (KEN 76) and identified as being finite and non-identical geometry and multiple scattering. Finite geometry is the difference between the ideal, infinitesimally wide beams used to derive the correction formula and the real rays used in the experiment (Fig. 2.8). The average attenuation for these paths will not be equal to that of the
Fig. 2.8 Diagram showing effect of finite beam width.
(From WEB 76)

Fig. 2.9 Diagram showing effect of non-identical geometry.
(From WEB 76)
central ray. Non-identical geometry is again due to finite beam width resulting in the scattering volume being larger than that defined by the transmission measurements (Fig. 2.9). A simple geometrical model and associated experiments suggested that these geometrical errors were small, of order 1%, and readily corrected for. Multiple scattering refers to photons being detected that have undergone more than one interaction and may have come from regions other than the volume of interest. This was estimated to cause an apparent increase in the density of up to 10%. A correction method was developed to overcome this problem based on the assumption that multiple scattering was dependent on the the dimensions and density of the sample under test as deduced from the lower energy transmission measurement compared to a reference standard. Though elegant this method does seem to introduce added complexity to the system.

Studies of multiple scattering have also been done by Huddleston et al (HUD 79a, 79b, 86) using a single source method, each time with a different radionuclide: $^{153}\text{Sm}$, $^{153}\text{Gd}$ and $^{192}\text{Ir}$. They concluded that the errors were indeed a function of the sample size and density in agreement with Kennet and Webber (KEN 76) but they recommended the use of empirically derived corrections. It was also found that the ratio of the multiple to single scattered photons depended on angle with smaller scattering angles giving the best results.

A clinical study using Webber’s Compton densitometer was carried out by Roberts et al (ROB 82). They found that the bone
density measured using this method correlated with age, weight and immobility in a similar way to the other methods of bone density determination. A very similar system using the more readily available $^{153}$Gd (103 KeV and 97 KeV) as the primary source with $^{170}$Tm again as the secondary was described by Piper and Preuss (PIP 76) though no in-vivo experiments were conducted.

The use of higher energy gamma-rays has been tried in-vivo, on the distal radius, by Hazen et al (HAZ 77) using a $^{137}$Cs (662 Kev) with a 90 degree scattering geometry. An empirically derived correction factor was applied to account for the attenuation effects, the factor being dependent on the thickness of soft tissue around the bone as deduced from a radiograph. The validity of this correction has been examined by Leichter et al (LEI 80), using models, who found that the effective attenuation of the water (representing soft tissue) surrounding the samples depended on the density of the scattering material. They felt, however, that it was still possible to produce calibration curves to account for these effects. Recently work has been published by the same group (LEI 87) on the use of a scanning Compton densitometer, based on this method, to discriminate between cortical and trabecular bone in the non-dominant distal radius. The system was capable of 1.8% precision for 2 mSv dose and was able to demonstrate that the spongiosa changed more rapidly with the onset of osteoporosis than did the cortical bone.

In an attempt to reduce the influence of multiple
scattering and to provide an alternative attenuation correction Huddleston et al (HUD 83, 85), developed a dual energy Compton densitometer which in many ways is an analogue of DPA. A two material model is assumed: the scatterer surrounded by a second material of different characteristics. By estimating the average scattering per electron and the effective attenuation of the materials, both of which depend on the given geometry and photon energies, and the path lengths the electron density can be found. The initial experiments were done using a $^{153}$Gd (effectively giving 100 KeV and 41 KeV) but the later work used $^{192}$Ir (317 and 468 KeV), the higher energies suffering less attenuation and considered more suitable for in-vivo study of the vertebrae. Only work on phantoms has been published to date but precisions of better than 1% have been achieved.

2.7.3 Coherent to Compton Scattering Ratio Bone Densitometry

The spectrum of scattered gamma-rays will contain both coherent and incoherent components, though a high resolution detector is necessary to distinguish them. It was suggested by Puumalainen et al (PUU 76) that if the Compton energy shift is small enough the attenuation for both the elastically scattered photons, which are at the primary energy, and the Compton scattered ones, at a lower energy, will be roughly the same and so taking the ratio of their intensities will give a quantity independent of any absorption due to overlying tissue.

If we consider a beam of photons, intensity $I_0$ incident
on a sample with a volume interaction, \( V \), containing \( n \) atoms per unit volume of an element atomic number \( Z \), then the coherently scattered intensity at angle \( \Theta \), \( S_{\text{coh}}(\Theta) \), and the equivalent inelastic intensity \( S_{\text{incoh}}(\Theta) \) will be given by:

\[
S_{\text{coh}}(\Theta) = I_0 \exp\left(-\int_{\text{int}} u(x) \, dx \right) \int \frac{d \sigma_{\text{coh}}(\Theta)}{d \Omega} \, n \, V \quad (2.32)
\]

\[
S_{\text{incoh}}(\Theta) = I_0 \exp\left(-\int_{\text{int}} u(x) \, dx \right) \int \frac{d \sigma_{\text{incoh}}(\Theta)}{d \Omega} \, n \, V \quad (2.33)
\]

where \( u(x) \) and \( u'(x) \) are the attenuation coefficients for the gamma-rays at their incident energy and after Compton scattering at angle \( \Theta \). Note that these are expressed as line integrals and are therefore general and valid even for inhomogenous materials surrounding the region of interest. If we now assume that these coefficients are equal, i.e. \( u(x) = u'(x) \) for all \( x \), then the ratio of coherent to Compton intensities, \( R_{\text{CC}} \), becomes, in the form factor approximation:

\[
R_{\text{CC}} = \frac{S_{\text{coh}}}{S_{\text{incoh}}} = \frac{(d \sigma_{\text{Th}}/d \Omega) |F(q, Z)|^2}{(d \sigma_{\text{KN}}/d \Omega) S(q, Z)} \quad (2.34)
\]

This ratio is clearly a function of the momentum transfer (i.e. photon energy and scattering angle) and the atomic number. Generally the former will be fixed in a given instrument and so it is the atomic number dependence that is of interest. Some
workers have taken the Thomas-Fermi approximation (equation 2.21) which gives a $Z^3$ form to the cross-section and also assumed a Compton cross-section proportional to $Z$ giving:

$$R_{cc} = \text{constant}.Z^3 / Z = \text{constant}.Z^2 \quad (2.35)$$

However it is clear from Fig. 2.10, taken from Bradley and Ghose (BRA 84) and based on modified form factors, that this ratio cannot be described in this way. At low momentum transfers the effects of shell closure are apparent and even at higher values the form is not that of a simple power dependence. It is only possible to say that the function $R_{cc}$, for a given photon energy and scattering angle, will be strongly dependent on the atomic number of the scatterer.

In the case of bone densitometry the material under examination is a region of trabecular bone and so rather than a single element being present $R_{cc}$ will be given by a weighted sum of the elements present:

$$R_{cc} = \frac{d_e \sigma^{Th}_{\theta}/d\Omega \cdot \sum_i (w_i/A_i) |F(q, Z_i)|^2}{d_e \sigma^{KN}/d\Omega \cdot \sum_i (w_i/A_i) \cdot S(q, Z_i)} \quad (2.36)$$

where $w_i$ is the proportion by weight of the $i^{th}$ element and $Z_i$ and $A_i$ are the associated atomic number and weight. Again from Fig. 2.10 it can be seen that the value of $R_{cc}$ will be greater the larger the proportion of higher atomic number elements present. Thus osteopenic bone with its reduced levels of calcium
Fig. 2.10 Z dependence of $G^2/S$ for various momentum transfers. (From BRA 84)

$G = \text{Modified form factor}$

$S = \text{Incoherent scattering function}$
(Z=20) and phosphorus (Z=15) will give a lower value of $R_{cc}$ than will healthy tissue. Unlike Compton scattering, however, it is not possible to relate the measured quantity directly to a simple physical parameter such as density. A further complication is that a real detector will collect the scattered spectrum over a range of solid angles and so strictly speaking equation 2.36 ought to be integrated over the angular acceptance of the detector.

The original experimental work (PUU 76) used $^{241}$Am (60 KeV) as the source, the scattered signal being measured at an angle of 90 degrees. The samples used were calcium hydroxyapatite powder distributed in paraffin wax. Rather than measure the area of the Compton peak in the scattered spectrum they used the peak height assuming this to be proportional to the area, this is not always the case as the width of the peak increases for higher Z elements due to electron motions (COO 82).

In-vitro studies were made of the os calcis by Kerr et al (KER 80) using a $^{153}$Sm (103 KeV) source and a 28 degree scattering angle. The smaller angle gives a higher count rate for the coherent signal improving the statistical precision but introducing problems in separating the peaks in the collected spectrum resulting from the two scattering mechanisms. These workers proposed that a system based on coherent scattering alone would prove to be more sensitive than the ratio of coherent to Compton to changes in bone mineral.

Stalp and Mazess (STA 80) conducted experiments using
solutions of $K_2HPO_4$ with $^{241}$Am for angles of 30 and 90 degrees and with a $^{153}$Gd source at 30 degrees and concluded that the latter configuration gave the best results in terms of statistical precision achieved. Nonetheless Olkkonen et al (OLK 81) continued to use $^{241}$Am and a 90 degree geometry in their study of distal radii taken from cadavers.

A series of experiments on scattering geometry, validity of the attenuation corrections and the effect of fat variation in the marrow was made by Ling et al (LIN 82). An $^{241}$Am source was used and though it was found that smaller angles gave a higher count rate they suggested that 90 degrees gave the most regular shape for the scattering volume making localisation of the region of interest easier. As for the attenuation corrections they concluded that overlying trabecular and cortical bone of normal thickness would not affect the ratio of coherent to Compton scattering but that too thick a layer of overlying tissue would cause an increase in $R_{cc}$ due to the greater attenuation of the lower energy, incoherent photons. The influence of fat variability was estimated by using excised bone suspended in solutions of tert-butyl alcohol of varying concentration. It was found that increasing alcohol led to an decrease in the value of $R_{cc}$.

Karellas et al (KAR 83) and Leichter et al (LEI 83) continued Ling's work at UCLA looking at the optimisation of the scattering angle. The quasi-theoretical side of their work was based on fitting a parameterisation of the form $z^{n-1}$ to the ratio
\( R_{cc} \) (equivalent to a \( Z^n \) form for the coherent cross-section) but as can be seen from Fig. 2.10 and the diagrams published in their own papers the value for \( n \) will depend on the momentum transfer and atomic number and so this approximation will only be valid for a limited range of \( Z \). These workers chose the range \( 8 < Z < 11 \) on the grounds that this was the "effective atomic number" for trabecular bone, but this approach must be treated with some caution as the significant elements as far as measured changes in \( R_{cc} \) are concerned are calcium and phosphorus (\( Z = 20 \) and 15) which are outside this range. From their calculations Karellas and Leichter concluded that higher momentum transfers, while giving poorer statistics due to the small coherent cross-section had a greater sensitivity to changes in the composition of the material under test. These two competing effects have to be optimised for a given geometry and Leichter (LEI 84) found that for a fixed angle (47 degrees) and three different photon energies (60, 81 and 140 KeV) scattering from \( K_2HPO_4 \) solutions that it was the lowest energy i.e. lowest momentum transfer that gave the best precision, indicating that it was the counting statistics that dominated. In contrast to this Karellas (KAR 83) found that for a fixed energy of 60 KeV the best measurement precision was for the larger angles indicating the reverse trend. Gigante and Sciuti (GIG 85b) have also chosen larger angles for their studies and in fact they adopted a backscattering geometry with an angle of 135 degrees. For this angle the coherent cross-section is very small but they claim the increased sensitivity makes up for the poor statistics. Two points that seem to be ignored in the literature with regard to these larger angles
are firstly that the increased Compton energy shift will lead to
greater differential attenuation between the elastic and
inelastic components rendering the attenuation correction invalid
and secondly that in a clinical environment time and dose
restrictions will favour the larger cross-sections found at
smaller angles. In fact in-vivo work published to date has
invariably quoted the moderate scattering angle of 71 degrees
(SHU 86, 87) and the recent in-vitro work of Hardie-brown (HAR
87) was done at an angle of 70 degrees.

The only in-vivo work published to date using coherent to
Compton scattering ratios has been carried out at UCLA using the
equipment developed by Karellas (KAR 83) employing 44 GBq of
\(^{241}\)Am (60 KeV) with a mean scattering angle of 71 degrees as
stated above. This apparatus was found to have a precision of 3%
and an accuracy of 5% for a typical measurement regime (SHU 85)
and a calibration system was developed using phantoms made of
varying quantities of bone ash suspended in petrolatum (LEI 85).
The in-vivo examination of the heel bones in a small group of
volunteers proved that the method could identify significant
differences in the average bone "density" for men and women and
an even more significant difference between healthy individuals
and a group of paraplegics (SHU 86). The absorbed soft tissue
dose was 3 mSv, but this is of course to a distal site, and the
measurement time was only 15 minutes per heel.

Further studies have recently been published (SHU 87) on
the variability of the results due to different locations of the
region of interest within the heel bone. It was found that the os
calcis was fairly homogeneous in the centre and that it was only at the edges when cortical bone was included in the interaction volume that significant variation occurred.

All the systems described above have used radio-nuclides as the photon sources with the associated limitations in flux. Puumalainen et al (PUU 82) did some work with an X-ray tube using caesium chloride as a critical absorber but no further work seems to have been published by this Finnish group on the use of X-ray sources. In the UK Webster et al experimented with a tungsten filter in association with an X-ray tube (WEB 85) and also a system of balanced erbium and ytterbium filters (WEB 86). It was found that satisfactory results could be obtained for a range of metal foils of different atomic numbers despite the relatively broad spectral lines and, of course, a much improved count rate was obtained. Unfortunately the method did not have sufficient discrimination to monitor changes in bone density (LIL 87). This group have now turned to a more conventional $^{241}\text{Am}$ source and 70 degree scattering angle (HAR 87) applying it to the problem of suitable phantom materials for such measurements.

2.7.4 Applications of Scattering in Other Fields

These techniques have also been applied in other fields both biomedical and industrial. A brief outline of some of these will be given.
Compton scattering as a method of measuring lung density has been investigated (KAU 76, KOU 80) but in-vivo measurements have proved to be inaccurate due, it is believed to multiple scattering and variable lung inflation (WEB 82). Imaging using Compton scattering has been developed largely as a non-destructive testing technique rather than a biomedical one but for further discussion on this the review of Holt (HOL 85) is recommended.

Coherent to Compton scattering ratios have been considered for assessing other biological materials rather than just bone. Puumalainen (PUU 77, 79) looked at its use to measure fat levels in the liver and also iodine (as a stable isotope) in tissues. Holt et al (HOL 83) used a Compton spectrometer to analyse some biological samples, unfortunately the apparatus had a fixed angle of 171 degrees and measurements took a very long time due to the small cross-section, but it was possible to demonstrate the sensitivity of the ratio $R_{cc}$ to changes in concentration of solutions. Schaetzler (SCH 79) applied the technique to the fat content of dairy products and meats finding a reasonable correlation between $R_{cc}$ and amount of fat present.

In metallurgy the coherent to Compton ratio has been used to monitor variations in alloy composition using both isotopic sources (CES 81, COO 82, CON 87) and also filtered X-rays (COO 85). The Warwick based group under Cooper have extended this filtered X-ray work to see if a low resolution detector with a suitable K-edge filter can be used to replace the high resolution
germanium detectors normally used. Similar work but using X-ray fluorescence as well as the ratio results has been done by Gigante and Sciuti (GIG 85a).

Manninen et al (MAN 84a,b) tried to develop a coherent technique to use Compton that would allow the "effective atomic number" of any material to be ascertained in an absolute manner. The problems of parameterisation have been considered already and the best that could be achieved was for atomic numbers of less than 20 and measurements had to be made at 120 degrees giving a low count rate.

Some of these methods have also been reviewed by Holt et al (HOL 84).

2.8 Comparison of Different Methods

The choice of method to assess bone density is a complex one and in many ways depends on which measurement site is considered to be the most important. Of the techniques reviewed the only strictly objective and quantitative ones that are in any way established as clinical tools are the absorptiometry techniques and CT. SPA only allows a measurement of the total bone present, trabecular plus cortical, in an appendicular site whereas DPA gives similar information for the axial skeleton. It is generally recognised that these two measurements are not well correlated (e.g. NIL 85, GEU 86) and that it is not possible to estimate the spinal bone mineral content from distal SPA scans.
It has been pointed out already that the spongiosa is generally more metabolically active than the cortical bone and would therefore be a better indicator of the onset of osteopenia. Thus the use of X-ray transmission tomography to image the spinal trabecular bone has potentially greater value than a DPA scan, and will also allow localised inhomogeneities to be identified. In fact it is found that there is reasonable correlation between these two methods (SAM 85). CT suffers from the problems of higher dose than DPA and marrow fat variability leading to errors in the measured values for the bone content, though it may be argued that DPA is only less sensitive to this variation because of its inherently poorer sensitivity to changes in trabecular bone. It is difficult to see X-ray transmission tomography having a useful role to play if some form of screening programme is to be considered for risk assessment, especially if equipment costs are also considered.

The use of $^{125}$I-CT enables the distal trabecular bone to be analysed but there is some doubt as to how well this correlates with the spinal spongiosa. Ruegsegger et al (RUE 81) found that for a small number of cadavers the two sites were strongly related but the in-vivo work of Sambrook et al (SAM 85) concluded that the correlation between distal and axial CT measurements was poor. It has been stated by Parfitt (PAR 87) that the appendicular trabecular bone, embedded in largely fatty marrow will, in fact, have a slower turnover than axial cortical bone in contact with active, red marrow.
One of the primary aims for bone mass measurements is, of course, to identify those individuals most in danger of suffering a fracture due to osteoporosis and a prospective study of 1098 women conducted by Wasnich et al (WAS 85) suggested that the best indicator of spinal fracture risk was in fact SPA scanning of the os calcis. This is contrary to what might be expected but as the study has continued the result has not changed (ROS 87). This probably indicates that the multifactorial nature of osteoporosis and associated fracture risk cannot be fully represented or assessed solely by spinal bone mineral levels.

If it is possible for SPA of a distal site to give better predictions than even axial DPA it is not unlikely that distal trabecular measurements may have as good if not better diagnostic potential. Thus techniques such as $^{125}$I-CT and photon scattering applied to the appendicular skeleton could provide a simple method of identifying individuals most at risk of suffering osteoporotic induced fractures.
3.1 Introduction

In order to study gamma-ray scattering and transmission tomography as possible bone densitometry techniques it is necessary to have suitable test objects. One option is to use excised bones but it is not possible to control their size, composition or homogeneity and their storage presents problems. An alternative is to use tissue substitute materials i.e. ones that have the same properties in terms of photon interactions as real bone and marrow. Using these tailor made test phantoms of given composition and dimensions can be made to allow calibration of apparatus and useful comparisons between methods.

The use of tissue substitutes in radiology is well established and White (WHI 78) has reviewed many such phantoms, with comments as to their applicability in various situations. The majority of tissue substitutes are formulated to provide the same photon absorption and electron stopping and scattering powers as the original tissue, at least for a given energy range (e.g. WHI 77a,b,c). However for certain applications more realistic tissue substitutes are required such as in this case where it is necessary to emulate the scattering cross-sections of bone tissue. Probably the best phantoms currently available are those that are termed "tissue equivalent" by Constantinou (CON 82) i.e. both the substitute and real tissue have the same elemental composition and density. In this way identical
radiation properties for both can be guaranteed, the only possible error that can then occur is due to subtle differences in chemical bonding. A wide range of such tissue equivalent materials have been developed by Constantinou and White (CON 82, WHI 82) and tested as dosimetry phantoms for a variety of different radiations. These workers use the term "tissue substitute" to mean materials that can represent real tissues in some circumstances but that do not necessarily fulfill the the stronger condition of being elementally equivalent.

If we consider gamma-ray scattering experiments then a number of different phantoms have been used. Perhaps the most popular has been potassium hydrogen orthophosphate (K$_2$HPO$_4$) which was originally suggested as an absorptiometry phantom but has nonetheless found extensive use in coherent to Compton ratio studies (STA 80, LIN 82, KAR 83, LEI 84, GIG 85b). It is of course not an elemental equivalent and as far as can be ascertained no real justification for its use as a scattering phantom has been published. More closely tissue equivalent phantoms have been made by distributing ashed bone in paraffin (PUU 76, LIN 82) or in petrolatum. These latter materials have been developed as a means of calibrating the in-vivo scattering equipment in use in California (SHU 85). The most recent work on scattering densitometry, published after the completion of the experimental work described in this thesis, is that of Hardie-Brown et al (HAR 87) who used the resin based phantoms developed by White et al (WHI 77c) to represent bone and soft tissue. They found reasonable but not perfect agreement between these phantoms
and real tissues, but these materials were formulated to match photon absorption, not scattering, and are not true elemental equivalents.

In the experimental work presented in this thesis several different phantom materials were used, these being derived from various sources. Some were formulated to be elemental equivalents but others would be classed merely as tissue substitutes. The choice of materials and the assessment of their suitability is discussed in the following sections.

3.2 Theoretical Considerations

In order to be able to justify a tissue equivalent or substitute it is necessary to know the elemental composition of the tissue being simulated and to calculate and compare the relevant radiation properties of the tissue and its proposed substitute. For the purposes of this work the important criteria are the differential cross-sections for coherent and Compton scattering and the linear attenuation coefficient for gamma-rays. To satisfy all these criteria successfully elementally equivalent phantoms are, clearly, to be preferred.

3.2.1 Elemental Composition of Bone and Marrow

The basic constituents of bone tissue have already been discussed and the point made that there is some variability in the composition of cortical bone (Woo 62) and that when
trabecular bone is considered, with its variable amounts of red and yellow marrow present, the biological variation in elemental content is considerable. The average composition for cortical bone usually quoted is based on the work of Woodard (WOO 62) who used excised bones from four young men for her chemical analysis. More recently a thorough study on the composition of bone and many different soft tissues has been carried out by Woodard and White (WOO 82 & 86, WHI 87) and it was the figures published in their initial paper (WOO 82) that were used for the calculations presented below and are given in Table 3.1. These figures are now out of date and should the calculations have to be repeated the latest tabulation (WHI 87) ought to be used. The differences between the old and new values are, however, fairly small (1% or less) and are merely due to extra data that has been collected.

3.2.2 Calculation of Radiation Properties

In order to determine the linear attenuation coefficients of the phantoms and the real tissues use was made of a program available on the University of Surrey computers that used the Jackson-Hawkes parameterisation (HAW 80) and the mixture rule (equation 2.24) to calculate the attenuation coefficient for a given combination of elements. For the purposes of this work an energy range of 25 to 110 KeV was used, covering the range of gamma-ray energies used in the experiments.

To enable the photon scattering properties of the real and substitute materials to be compared the partial differential
attenuation coefficients for coherent and Compton scattering were calculated using a simple BASIC program adapted from the one originally used by Kerr et al (KER 80). These coefficients are the contributions of the given scattering process to the total attenuation and are defined as:

\[
\sigma_{\text{coh}}(\theta) = p N_A \sum_i w_i \frac{d \sigma^{\text{Th}}}{d \Omega} F(q, Z_i) \]

\[
\sigma_{\text{incoh}}(\theta) = p N_A \sum_i w_i \frac{d \sigma^{\text{KN}}}{d \Omega} S(q, Z_i) \]

where \( p \) is the density, \( N_A \) is the Avogadro constant, \( w_i \) is the fraction by weight of the \( i \)th element and \( Z_i \) and \( A_i \) are the atomic number and weight respectively. \( F(q, Z) \) and \( S(q, Z) \) are the atomic form factors and scattering factors discussed in section 2.7.1, the values of which were taken from the tabulations of Hubbell et al (HUB 75). These partial attenuation coefficients can be interpreted as the probability of a photon being scattered through an angle \( \theta \) by the given mechanism (coherent or Compton scattering) per unit path length of material. The calculations were performed for photons of energy 60 KeV and 100 KeV corresponding to the \(^{241}\text{Am}\) and the \(^{153}\text{Gd}\) gamma-ray energies used in the experiments. The ratio \( R_{\text{cc}} \) was given by the ratio of the two partial differential attenuation coefficients.
Table 3.1 Elemental Composition of bone and marrow (% by weight)

<table>
<thead>
<tr>
<th>Element</th>
<th>Z</th>
<th>Cortical Bone</th>
<th>Red Marrow</th>
<th>Yellow Marrow</th>
<th>Spongiosa</th>
</tr>
</thead>
<tbody>
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<td>H</td>
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</tr>
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<td>0.68</td>
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<td>44.28</td>
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<tr>
<td>Mg</td>
<td>12</td>
<td>0.21</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
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<td>P</td>
<td>15</td>
<td>10.20</td>
<td>0.19</td>
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<td>0.14</td>
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<td>-</td>
<td>-</td>
</tr>
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<td>-</td>
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<td>0</td>
<td>0.08</td>
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</tr>
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Relative Density 1.90 1.03 0.98 1.18

Taken from Woodard & White (WOO 82).
3.3 Cortical Bone Substitutes

3.3.1 Liquid Substitutes

Constantinou in his study of liquid and gel phantoms (CON 82) concluded that the best liquid substitute for cortical bone was a concentrated solution of $K_2HPO_4$ (160 g to 100 ml of water). The potassium ($Z=19$) in this compound replaces the calcium ($Z=20$) that is found in real bone. Any attempts to add trace elements to this substitute to improve its elemental composition result in precipitates from the solution. As has already been discussed such solutions have proved popular as bone phantoms for many scattering experiments with little real justification as to their suitability in terms of scattering cross-sections. The experimentally determined relative density of such solutions was found to be 1.70, in slight disagreement with the value of 1.68 quoted by Constantinou (CON 82). The former figure was used to calculate the linear attenuation and differential attenuation coefficients discussed above, and the results are displayed in Figs. 3.1 - 3.3. It can be seen that the $K_2HPO_4$ solution behaves very much like cortical bone in its scattering cross-sections as well as total attenuation thus making it a useful simulator of osseus tissue in many experiments. It must be borne in mind, however, that it has a relative density of only 1.70 compared with 1.90 for cortical bone hence making $K_2HPO_4$ solution unsuitable as a means of directly calibrating gamma-ray scattering apparatus for bone density (LEI 85).
Fig. 3.1

Cortical Bone  --- \( \text{K}_2\text{HPO}_4 \)  --- \( \text{BEP}2 \)
Fig. 3.2a

Rcc for Bone and Bone substitutes

60 KeV

---

- Cortical Bone
- K$_2$HPO$_4$
- BEP2

Fig. 3.2b

Rcc for Bone and Bone Substitutes

100 KeV

---

- Cortical Bone
- K$_2$HPO$_4$
- BEP2
Fig. 3.3

Muh coherent for bone & bone substitutes

60 KeV

- Cortical Bone
- K₂HPO₄
- BEP2

100 KeV

- Cortical Bone
- K₂HPO₄
- BEP2
3.3.2 Powder Substitutes

Some of the preliminary experiments were done using calcium carbonate and wax mixtures as bone substitutes, these being based on the work of Bradley et al (BRA 85), but transmission measurements indicated that these were far from homogenous and so no further work was done with them.

As an alternative, a tissue equivalent material developed at the University of Surrey by Smith and Jackson (SMI 87b) for pion dosimetry, was adopted. The interactions of pions with matter are dependent on the atomic pion capture cross-sections which are sensitive to molecular environment, and then, following capture, on the nuclear absorption of the mesons. This makes for a very stringent set of conditions that has to be met by phantom materials requiring not only elemental equivalence but also similarities in molecular structures. The substitute chosen was designated by its developers "bone equivalent powder 2" (BEP2) and its composition is given in Tables 3.2 & 3.3. They found its relative density to be only 0.5 but they made no attempt to compact it. For this thesis, however, attempts were made to compress BEP2 in a hydraulic press and it was found possible to produce pellets with a diameter of 20 mm and a consistent relative density of 1.37. This is still less than that of real cortical bone by some margin despite being elementally equivalent and thus indicates that air gaps were still present in the pellets. Measuring its density using Archimedes' principle gave its relative density as $2.03 \pm 0.02$, a figure slightly greater
than the average value quoted for cortical bone. As the BEP2 was
to be used distributed in marrow substitute materials such that no
air gaps would remain it is this last figure that was used in
calculating the radiation properties of the material, and the
results are shown in Figs. 3.1 - 3.3. It can be seen that this
tissue equivalent has attenuation and scattering properties
closely matched to those of cortical bone, which coupled with its
reasonable density when in a mixture, makes it eminently suitable
to represent the hard bone component in spongiosa phantoms.

3.4 Bone Marrow Substitutes

In order to represent trabecular bone it is necessary to
have a bone marrow substitute in which to dilute or suspend the
cortical bone equivalent. Two avenues were explored: a liquid to
be used in association with the $K_2HPO_4$ and a gel for use with the
BEP2.

3.4.1 Liquid Substitutes

A liquid substitute for bone marrow proved to be a
non-trivial task. Constantinou (CON 82) does not recommend any
suitable phantom material and in association with White (WHI
82) suggests some formulations but with some doubts as to their
accuracy. After some calculations based on the method used by
these workers (CON 82) a red marrow liquid (RML) was adopted,
derived from the mixture RM/L3 given by Constantinou (CON 78),
but without the trace elements as these would only give rise to
precipitates when combined with the $\text{K}_2\text{HPO}_4$ solution. RML is a simple solution of water, glycerol and urea its composition being given in Tables 3.2 & 3.3. It has a relative density of 1.09 which has to be compared with a mean value for red marrow of 1.03 (WOO 82). The relevant radiation properties are displayed graphically in Figs. 3.4 – 3.6. It can be seen that it does not have the ideal properties with its attenuation coefficient and scattering cross-sections approximately 5% greater than those of red marrow. Nonetheless it has to be considered the best that can be readily achieved.

It had been hoped that a suitable substitute for yellow marrow could be made to allow an investigation into the influence of fat on the scattering and tomography techniques but attempts by Constantinou (CON 82) to formulate suitable materials that were also miscible with water failed, suggesting that this was a difficult problem. Nonetheless some attempts were made to use 2 methyl propan-2-ol (tert-butyl alcohol) as employed by Ling et al (LIN 82) but, while stable in aqueous solution on its own, it was not miscible with $\text{K}_2\text{HPO}_4$ solution.

3.4.2 Gel Substitutes

As mentioned above petrolatum has been recommended (LEI 85) as a marrow substitute for gamma-ray scattering experiments and it was clearly appropriate to produce a set of similar phantoms. Unfortunately petrolatum is not a well defined material being in fact a family of micro-crystalline
Table 3.2 Composition of Bone and marrow substitutes

<table>
<thead>
<tr>
<th>Material</th>
<th>Composition (% by weight)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BEP2</td>
<td>Calcium Phosphate Tribasic (Hydroxyapatite) (59.0%), Gelatin (3.0%), Glutamine (20.6%), Glucose (17.4%)</td>
</tr>
<tr>
<td>RML</td>
<td>Water (65.0%), Glycerol (30.2%), Urea (4.8%)</td>
</tr>
<tr>
<td>MSG</td>
<td>Water (75.3%), Gelatin (19.4%), ethanol (5.3%)</td>
</tr>
</tbody>
</table>

Table 3.3 Elemental Composition of Substitutes

<table>
<thead>
<tr>
<th>Element</th>
<th>Z</th>
<th>BEP2</th>
<th>RML</th>
<th>MSG</th>
<th>Petrolatum</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
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<td>2.8</td>
<td>10.2</td>
<td>10.4</td>
<td>14.7</td>
</tr>
<tr>
<td>C</td>
<td>6</td>
<td>16.8</td>
<td>12.8</td>
<td>12.4</td>
<td>85.3</td>
</tr>
<tr>
<td>N</td>
<td>7</td>
<td>3.9</td>
<td>2.2</td>
<td>3.6</td>
<td></td>
</tr>
<tr>
<td>O</td>
<td>8</td>
<td>42.2</td>
<td>74.8</td>
<td>73.6</td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>15</td>
<td>10.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ca</td>
<td>20</td>
<td>22.2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Measured Relative Density

|          | 2.03 | 1.09 | 1.06 | 0.88 |
Fig. 3.4

- Red Marrow
- Yellow Marrow
- RML
- MSG
- Petrolatum
Fig 3.5

Rcc for marrow & substitutes

60KeV

- Red Marrow
- Yellow Marrow
- RML
- MSG
- Petrolatum

Rcc

Rcc for marrow & substitutes

100KeV

- Red Marrow
- Yellow Marrow
- RML
- MSG
- Petrolatum
Fig 3.6

Muh coherent for marrow & substitutes

60 KeV

- Red Marrow
- Yellow Marrow
- RML
- MSG
- Petrolatum

100 KeV

- Red Marrow
- Yellow Marrow
- RML
- MSG
- Petrolatum
hydro-carbon waxes with chemical formulae from $C_{38}H_{78}$ to $C_{42}H_{86}$ (HAW 77) and relative density in the range 0.815 to 0.880. Thus it is elementally rather different to bone marrow having no oxygen or nitrogen and with a density below even the 0.98 expected for yellow marrow. It is also worth noting that some of the products sold as petrolatum are actually blends of lighter and heavier hydro-carbons to give a mixture that approximates to the genuine thing. Such variability and uncertainty in composition raises doubts as to the suitability of petrolatum as a tissue substitute, especially if being considered as a calibration standard. For the phantoms made in this work the petrolatum purchased was found to have a relative density of 0.882 ± 0.005 and to calculate its attenuation and scattering coefficients was assumed to have an average formula of $C_{40}H_{82}$. The results of the calculations are displayed in Figs. 3.4 - 3.6 where it can be seen that petrolatum is not even similar to yellow marrow and is certainly not an ideal substitute for bone marrow with an attenuation coefficient 10% less than that of yellow marrow.

A common gel tissue substitute is based on a water and gelatine mixture (e.g. CON 82, SMI 87b), gelatine being formed from the hydrolysis of collagen and hence having a composition and density that is both well defined and similar to that of protein. The tissue equivalent gel developed for these experiments was based on Constantinou’s MSG1 (CON 82), a muscle substitute made of water, gelatine and ethanol, see Table 3.2. The alcohol acts as an anti-bacterial agent increasing the life of the phantom. The measured relative density of the MSG was
1.06, this is to be compared with the mean value for red marrow of 1.03 (Woo 82). To calculate the radiation properties this value of 1.06 was used along with an assumed formula for gelatine of $C_{76}H_{124}O_{29}N_{24}S$ (GRA 69). The results are displayed in Figs. 3.4 - 3.6. It can be seen that MSG has properties closer to those red marrow than the other substitutes though the agreement cannot be considered perfect.

3.5 Experimental Phantoms

As discussed above the phantoms that were manufactured for use in these experiments can be considered under the broad headings of liquid phantoms, based on $K_2HPO_4$, or gel phantoms, using BEP2 as the bone substitute suspended in MSG or petrolatum.

3.5.1 Liquid Phantoms

Manufacture of the liquid phantoms did not present any major problems. The use of a digital balance allowed very precise (error $< 0.1\%$) control of the masses of the chemicals used, these being, where possible, "Analar" grade supplied by BDH Ltd. Care had to be taken when using the $K_2HPO_4$, however as it is hygroscopic and once exposed to the atmosphere rapidly becomes contaminated so that a given mass will actually contain an unknown proportion of water. To overcome this problem the $K_2HPO_4$ was not stored as a powder but, once a sealed container was opened, was made into a "stock" solution of the correct concentration to represent cortical bone. All such solutions were
made using de-ionised water, an accidental use of the local tap water on one occasion caused a small, but noticeable, amount of precipitate to form.

The simplest liquid phantoms were merely aqueous solutions of $\text{K}_2\text{HPO}_4$ of varying concentrations as used by other workers. Several such sets of solutions were made for use in this work and were contained in polythene bottles with nominal diameters of 40 or 50 mm depending on the experiment. The initial set produced were referred to as P1 to P7 and covered the range from pure water to a saturated solution thus effectively representing even cortical bone. Later batches, designated BL1 to BL11 and BL21 to BL31 had densities in the range 1.00 to 1.40 in an attempt to represent trabecular bone.

It should be noted that being solutions and not just mixtures the linear attenuation coefficients of these phantoms do not have a perfectly linear dependence on the mass of $\text{K}_2\text{HPO}_4$ per unit volume, as can be seen from Fig. 3.7 where a small deviation from a straight line is apparent. The attenuation coefficients for this graph were calculated from the mixture rule using the experimentally determined relative densities of the solutions, the mass per unit volume of the phosphate being given by this density multiplied by the weight fraction of $\text{K}_2\text{HPO}_4$. This non-linearity results from the fact that the volumes of the two components are not strictly additive i.e. a given volume of phosphate will not displace an identical volume of water.
Slightly more realistic liquid phantoms were produced by adding the \( K_2HPO_4 \) cortical bone substitute to the RML bone marrow equivalent. The resulting phantoms were called TBL1 to TBL7 and had relative densities from 1.09 to 1.48, again emulating the range from pure marrow to spongiosa with a higher bone content than normal.

Quality control of the liquid phantoms was also straightforward as their homogeneity was guaranteed. The use of a relative density bottle enabled a fast and accurate check on the density of the solutions to be made, the reproducibility of this measurement was significantly better than 0.5%. This method proved its efficacy when a batch of \( K_2HPO_4 \) that had been contaminated by atmospheric moisture was rapidly identified because it produced density values inconsistent with previous results using fresh phosphate.

3.5.3 Gel Phantoms

The preparation of the BEP2 for use as the bone equivalent in these phantoms involved the thorough mixing of several powders. This was achieved by blending the powders for a couple of hours in a ball mill. This is a jar, containing various sizes of ceramic marbles, that is kept rotating on a set of revolving rollers. The MSG was made according to the method of Constantinou (CON 82) but unfortunately no facilities were available to stir the gel under vacuum. This was not a problem for the pure gel but did cause problems when the BEP2 was added.
to the MSG as air trapped in the powder was difficult to expel.

The initial work on the gel phantoms was done in collaboration with Douskas and formed part of his MSc (DOU 87). To achieve thorough dispersion of the BEP2 within the phantoms the gels were used in a molten state. For the petrolatum this was simply a case of warming it up but for the MSG it was necessary to use it immediately after manufacture before it had a chance to solidify. In both cases the liquified gel and required amount of BEP2 were placed in medium gauge polythene bags that were then heat sealed. The resulting phantoms were cylinders, nominally 40 mm in diameter and 60 mm long. Due to the viscosity of the MSG it was found difficult to ensure total expulsion of the air from the mixture, especially when a large proportion of the bone equivalent powder was needed, highlighting the need for mixing under vacuum.

Douskas produced two sets of phantoms: the PEPHA series using petrolatum as the soft tissue base emulating Leichter et al (LEI 85), and the GEPHA set using MSG as a marrow equivalent. The mass of hydroxyapatite per unit volume (i.e. the effective bone mineral content) for both sets ranged from 0 to 270 Kg/m$^3$ compared with an average value of 230 Kg/m$^3$ for normal spongiosa (WOO 82), thus comfortably spanning the required range.

Unlike the liquid phantoms great care had to be taken to ensure that these phantoms were indeed homogeneous, i.e. that
there were no non-uniformities in the distribution of BEP2 and that there was no air trapped within the mixture. The initial test applied was again to measure the density of the phantoms. This was not as easy as it had been for the liquids but it was nonetheless readily accomplished using a large relative density bottle with the necessary corrections being made for the polythene wrapping around the phantoms giving an overall reproducibility of better than 1%. The density of a mixture of components with densities $p_i$ and weight fractions $w_i$ is given by:

$$p = \left( \sum_i w_i/p_i \right)^{-1}$$

and departures from the values predicted by this formula indicate some form of contamination. When applied to the phantoms made by Douskas it was found that the PEPHA phantoms had densities that obeyed eqn. 3.3 but that the GEPHA phantoms had values up to 15% lower than predicted indicating the presence of trapped air. This air present in the phantom is not a problem for coherent to Compton scattering studies as it is the proportions of the different elements not the overall density that is measured (eqn. 2.36), but for coherent scattering (eqn. 2.32) and for CT (eqn. 2.23) the measured quantity is dependent on the density and thus such contamination will lead to erroneous results.

The first test applied to the phantoms was that recommended by Leichter et al (LEI 85), that is to take coherent to Compton scattering measurements of different regions within
the material checking that consistent results are obtained. Douskas found that both sets of phantoms appeared to be homogeneous with the scattering ratio, $R_{cc}$, from the different zones agreeing within statistical errors.

A second method of testing was to use the CT apparatus described in Chapter 5. This produced cross-sectional images of the phantoms and any gross inhomogeneities of large air bubbles present would be clearly visible. Also the average linear attenuation of different regions within the phantom could be compared, any non-uniformities in BEP2 distribution would give rise to variations in photon attenuation. The averaging had to be done over a reasonable number of pixels, usually of order 100 to ensure a reasonable precision, the uncertainty associated with this average value was the standard error of the mean given by (BEV 69):

$$\sigma_{\text{mean}} = \frac{\sigma}{\sqrt{N}} \quad (3.4)$$

where $N$ is the number of pixels being averaged and $\sigma$ is the standard deviation. By taking a large enough region this error was of the order of 0.5-1%. Douskas found that for the GEPHA phantoms different regions in the phantom had the same attenuation coefficient within the given errors but unfortunately the GEPHA phantoms, especially the denser ones, proved to have an unacceptable degree of inhomogeneity with regions differing in mean attenuation by up to 5 standard errors of the mean. An alternative way of using the CT images to test the homogeneity of
he phantoms was to look at the frequency distribution of the pixel values, and any inhomogeneities should lead to a broadening of this distribution but in practise it was to be an insensitive test.

The PEPHA phantoms prepared by Douskas were considered acceptable for use in the bone-mass measuring experiments but the GEPHA phantoms were too inhomogeneous and clearly suffered from air contamination. As a result the author had to prepare a further batch of MSG/BEP2 mixtures called GB phantoms. This time great care was taken to try to expel all the air from the phantoms prior to heat sealing the polythene. Also rather than being left to stand while they gelled, giving the BEP a chance to settle to the bottom, the phantoms were placed on a slowly rotating jig. Repeating the density measurements gave good agreement between the measured and predicted densities with only one phantom, the one with the highest BEP2 content, being 3% less than expected (Table 3.4) indicating air trapped in the mixture. The CT study of the phantoms gave reasonable uniformity with variations being of order 3% or less, but again there was a problem with the densest phantom which had an air bubble trapped within it. The scattering measurements were not repeated as Douskas (DOU 87) had not found them sensitive to the inhomogeneities in his GEPHA phantoms.

The use of BEP2 and MSG to produce trabecular bone phantoms cannot be considered a complete success due to the problems of inhomogeneity and of air being trapped within the
Attenuation of K2HPO4 Solution

Mass of K2HPO4 per unit volume / Kg m⁻³

Fig. 3.7
Table 3.4 Composition, Density and Mineral Content of Phantoms

<table>
<thead>
<tr>
<th>Phantom</th>
<th>% Weight</th>
<th>% Weight</th>
<th>Calculated R.D.</th>
<th>Measured R.D.</th>
<th>BMC* (Kg/m³)</th>
</tr>
</thead>
<tbody>
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<td>100.0</td>
<td>-</td>
<td>-</td>
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<td>0</td>
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<tr>
<td>PEPHA1</td>
<td>90.5</td>
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<td>0.932</td>
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<td>52</td>
</tr>
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<td>81.8</td>
<td>18.2</td>
<td>0.983</td>
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<td>70.2</td>
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<td>1.056</td>
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<td>PEPHA4</td>
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<td>1.142</td>
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</table>

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<th>Phantom</th>
<th>% Weight</th>
<th>% Weight</th>
<th>Calculated R.D.</th>
<th>Measured R.D.</th>
<th>BMC* (Kg/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSG BEP2</td>
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<td>-</td>
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</tr>
<tr>
<td>GB1</td>
<td>90.9</td>
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<td>1.10</td>
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<td>59</td>
</tr>
<tr>
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<td>1.14</td>
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</tr>
<tr>
<td>GB3</td>
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<td>28.4</td>
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<td>201</td>
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<td>GB4</td>
<td>61.9</td>
<td>38.1</td>
<td>1.30</td>
<td>1.26</td>
<td>283</td>
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</tbody>
</table>

* BMC is defined as the mass of hydroxyapatite per unit volume (eqn. 3.6)
material. It may be that these problems could be overcome by using vacuum mixing as recommended by White and Constantinou (WHI 82). While the PEPHA phantoms gave fewer problems in manufacture their tissue equivalence is open to question and are certainly not ideal trabecular bone substitutes.

A final point to be made about these materials is that, being mixtures not solutions, their linear attenuation coefficients will be a linear function of the mass of hydroxyapatite per unit volume. This follows from the mixture rule (eqn. 2.24) and eqn. 3.3 which can be combined to give:

\[
\begin{align*}
    u &= (w_h \rho_h) \frac{u_h - u_s}{\rho_h + u_s} \\
    &(3.5)
\end{align*}
\]

where \(u\) and \(\rho\) are the linear attenuation coefficient and density for the mixture, the subscripts \(h\) and \(s\) signifying these same quantities for the hydroxyapatite and soft tissue components respectively, and \(w_h\) being the proportion by weight of hydroxyapatite. If we define bone mineral content (BMC) to be the mass of hydroxyapatite per unit volume (i.e. \(w_h\rho\)) then we have:

\[
\begin{align*}
    \text{BMC} &= w_h \rho \\
    &(3.6)
\end{align*}
\]

\[
\begin{align*}
    u &= \text{BMC} \frac{u_h - u_s}{\rho_h + u_s} \\
    &(3.7)
\end{align*}
\]

i.e. the attenuation coefficient is linearly proportional to the bone mineral content. Similarly it can be shown that a similar
linear relationship holds for the scattering cross-sections e.g. for coherent scattering:

\[ u_{coh} = \frac{BM C ((u_h^{coh} - (u_s^{coh})}{p_h + (u_s^{coh})} \quad (3.8) \]

3.6 Conclusion

Several trabecular bone substitutes have been adopted or developed for use in these experimental studies. None of them, however, can be considered ideal but each has its uses. The liquid phantoms are easy to make, have guaranteed homogeneity and their composition can be accurately controlled though they fall short of being elementally equivalent to trabecular bone. On the other hand the gels are elementally identical to spongiosa but this is at the price of reduced homogeneity and greater uncertainty in composition.
CHAPTER 4 GAMMA-RAY SCATTERING EXPERIMENTS

4.1 Introduction

The main aim of the experiments presented in this chapter was to develop a technique, ultimately for use in bone densitometry, based on coherent gamma-ray scattering as proposed by Kerr et al (KER 80). They suggested that in the more usual coherent to Compton method, as the numbers of elastically and inelastically scattered photons are both dependent on the bone mineral concentration, the ratio of the two will be less sensitive to changes in this concentration than the number of coherently scattered photons alone. To be able to use the elastic component in the scattered photon spectrum it is necessary to make corrections for the attenuation of the gamma-rays in the surrounding material, in the same way as in the Compton scatter densitometry method reviewed in chapter 2. In this case, however, it is simpler as there is no change in the photon energy and thus the need for a secondary source is removed, the primary one may be used. Consider the arrangement in Fig. 4.1: for the first source position the coherent scattering, $S_1$, recorded in detector 1 and the transmitted signal, $T_1$, recorded in detector 2 will be:

$$S_1 = I_0 \exp\left(-\int_a^b u(x)dx\right) \frac{d}{d\Omega} \sigma^\text{coh}(\Theta) n V$$

$$ \cdot \exp\left(-\int_c^d u(x)dx\right)$$

$$T_1 = I_0 \exp\left(-\int_a^b u(x)dx\right) \exp\left(-\int_b^0 u(x)dx\right)$$

(4.1)  

(4.2)
Fig. 4.1 Attenuation Correction
By Transmission

Source

Detector 2

Detector 1

Source

Detector 2

Detector 1
where the symbols have the same meanings as for equation 2.32. With the source in the second position the scattered and transmitted signals, \( S_2 \) and \( T_2 \), are:

\[
S_2 = I_0 \exp\left( -\int_a^b u(x) \, dx \right) \exp\left( -\int_0^\infty c(x) \, dx \right) \tag{4.3}
\]

\[
T_2 = I_0 \exp\left( -\int_a^b u(x) \, dx \right) \exp\left( -\int_0^\infty c(x) \, dx \right) \tag{4.4}
\]

When combined these give:

\[
R_{ct} = \left( \frac{S_1}{S_2} \right)^{1/2} = \frac{d \, \alpha^{\text{coh}}(\theta)}{d \Omega} \tag{4.5}
\]

The count rate for the transmission measurements will, in general, be much greater than the number of photons being scattered and so it will be the latter that will limit the statistical precision of this ratio \( R_{ct} \). This attenuation correction will of course suffer from the same problems of finite and non-identical geometry and multiple scattering experienced in the Compton scatter densitometers and is only rigorously valid for infinitesimally thin beams.

4.2 Experimental Apparatus

The essential units for scattering experiments are a suitable detector, with associated electronics, a source of
photons and a pair of collimators to define the volume of interest (Fig. 4.2).

4.2.1 Detector and Electronics

To be able to discriminate between the coherent and Compton peaks in the scattered photon spectrum it is necessary to use a high resolution detector. The energy difference between the elastic and inelastic scattering components for an incident photon energy of 60 KeV is 6.3 KeV at 90 degrees and 4.3 KeV for an angle of 70 degrees. A typical sodium iodide (NaI(Tl)) scintillation detector would have a full width half maximum (FWHM) resolution of about 7 KeV at this energy and would not therefore be able to separate the two signals. Only a semi-conductor detector is capable of resolving the coherent from the Compton scattering with a high enough efficiency to be practicable.

The detector used in this work was a high purity germanium (HpGe) supplied by Princeton Gamma-Tech with a nominal active volume of 200 mm$^2$ by 10 mm deep, fitted with a beryllium window to allow low energy (<10 KeV) spectroscopy. The germanium crystal has a lithium diffused contact on one face that effectively dopes this side of it to form a large diode. When a reverse bias is applied the depletion region occupies the full width of the detector due to the small number of impurities present in the germanium. To restrict the number of thermally generated charge carriers being created while under bias it is
Figure 4.2 Detector and collimators

Figure 4.3 Detector and associated electronics
necessary to keep the crystal in a liquid nitrogen cooled cryostat. Photons interacting within this depletion region will give rise to electron-hole pairs, the number of which depends on the energy deposited, and these will drift under the influence of the applied electric field to the end contacts of the crystal. Here a charge sensitive pre-amplifier, with the initial stage cooled in the cryostat to limit noise, converts this signal into a voltage pulse. The production of electron-hole pairs is a statistical process and so the number generated is subject to a certain spread in values. More detailed discussion of solid state detectors can be found in the works by Knoll (KNO 79) and Ewan (EWA 79).

The associated electronics for the detector are shown in Fig. 4.3. As the detector uses a pulsed optical feedback pre-amplifier, which has a sawtooth rather than a DC level baseline, the amplifier has to be one with an active baseline restoration circuit. Pulse processing was done by the multi-channel analyser (MCA) which digitises the output of the amplifier, storing and displaying the results for analysis. Spectra could be transferred from the MCA to the BBC micro-computer using the serial communications port and stored on floppy disc. Special software was written in machine code using the assembler resident in the BBC BASIC language to make this data transfer as rapid as possible. A 1K spectrum could be written to disc in under one minute, the old BASIC code in use before took about five times as long. From the micro-computer it was possible to communicate with the University of Surrey Prime
computers using various terminal emulation packages; the latest and most reliable being the KERMIT public domain program.

A study of the detector's characteristics was considered an important preliminary experiment as the device was a recent purchase and had not been previously examined.

4.2.1.1 Detector Efficiency

The efficiency of a detector can be defined in terms of its intrinsic efficiency; the number of photons of a given energy detected as a fraction of the number incident on the active volume, or, for a given geometry, as the absolute efficiency i.e. the number detected as a fraction of the total number emitted by the source. As the exact position of the crystal within the cryostat was not known the absolute efficiency was chosen.

A number of papers have been published on methods for establishing the efficiency of low energy gamma- and X-ray detectors, both HpGe and lithium drifted silicon, (e.g. DEB 83&85, BAR 84, CAM 86, RIE 87). The technique chosen has been used before at Surrey (KER 78) and uses a light perspex frame to hold the standard "wafer" sources at a fixed, reproducible distance from the detector and is similar to that employed by Moens and Hoste (MOE 83). The radionuclides used were supplied some years previously by Amersham International PLC and so only the longer lived ones were suitable. A review of the literature
<table>
<thead>
<tr>
<th>Radio-nuclide &amp; half life</th>
<th>Energy</th>
<th>Intensity</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cs-137</td>
<td>10964(90) days</td>
<td>32.06 (Kα)</td>
<td>0.0565(7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>36.4 (Kβ₁)</td>
<td>0.0109(14)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>37.3 (Kβ₂)</td>
<td>0.00274(6)</td>
</tr>
<tr>
<td>Am-241</td>
<td>432.9(8) years</td>
<td>11.9 (L₁)</td>
<td>0.0086(3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13.9 (Lα)</td>
<td>0.133(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17.8 (Lβ₁)</td>
<td>0.194(6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20.8 (Lγ)</td>
<td>0.049(2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>26.35</td>
<td>0.024(1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>59.54</td>
<td>0.3582(12)</td>
</tr>
<tr>
<td>Co-57</td>
<td>271.80(4) days</td>
<td>6.396 (Kα)</td>
<td>0.502(14)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.06 (Kβ)</td>
<td>0.0691(20)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14.41</td>
<td>0.093(2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>122.06</td>
<td>0.8563(15)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>136.33</td>
<td>0.1075(30)</td>
</tr>
<tr>
<td>Ba-133</td>
<td>3841(5) days</td>
<td>30.85 (Kα)</td>
<td>0.9946(124)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>35.4 (Kβ)</td>
<td>0.2316(25)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>53.2</td>
<td>0.0218(3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>79.6/81.0</td>
<td>0.362(6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>160.6</td>
<td>0.00642(17)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>223.1</td>
<td>0.00468(10)</td>
</tr>
</tbody>
</table>
was made to compile Table 4.1 showing the intensities of the various photon energies.

To find the photopeak areas in the recorded gamma-ray spectra a modified version of the peak fitting program SAMPO (ROU 69, CAR 77) was used. This fits a Gaussian lineshape, with exponential tails and a polynomial background, to statistically significant peaks. The user defines a number of single, isolated lines that can be reliably analysed and the resulting parameters are stored in a table. The shape parameters of all remaining peaks in the spectrum are then found by interpolating between these tabulated values, enabling multiplets to be fitted with a reasonable degree of certainty. As with all such packages it is necessary to examine the output of the program, especially the Chi-squared of the resulting fit and the graphs comparing the data and the fitted shapes to ensure that reasonable functions are being used. Some of the X-ray multiplets, especially for $^{241}$Am required two or three attempts before satisfactory results were obtained. Campbell (CAM 82) has suggested that the quality of the fits produced by such programs can be assessed by considering the ratio of the areas assigned to the 79.6 and 81.0 KeV doublet in the $^{133}$Ba spectrum. The accepted value for this ratio is $0.0777 \pm 0.0005$ and for the SAMPO output in this experiment it was found to be $0.0776 \pm 0.0012$ indicating that the program was performing satisfactorily.

The absolute efficiency for 50 mm source to detector window separation is given in Table 4.2 and displayed as a graph.
in Fig. 4.4. The errors are plus or minus one standard deviation and were calculated by adding in quadrature the individual uncertainties in the source activities, gamma-ray intensities, fitted peak areas and the estimated error in source positioning. This latter quantity was found by collecting ten separate spectra from an $^{241}$Am source, removing and replacing it between each one. The spread in the areas fitted to the 59.6 KeV peak was consistent with the error due to counting statistics added in quadrature to a further error of 0.9%, and this was taken to be the uncertainty in positioning. To take account of the decay of the radio-nuclides the uncertainties in their activities, $\sigma_{A\%}$, were calculated as:

$$ (\sigma_{A\%})^2 = (\sigma_{A0\%})^2 + (\sigma_{t1/2\%} t \ln 2)^2 $$

(4.6)

where $\sigma_{A0\%}$ and $\sigma_{t1/2\%}$ are the errors in the initial activity and the half-life, as percentages, and $t$ is the time elapsed since the source was calibrated.

It can be seen from Fig. 4.4 that the efficiency has a broad maximum for the range of energies from 50 to 60 KeV, the region of interest when considering the scattering of 59.5 KeV gamma-rays from $^{241}$Am. Using estimated dimensions for the crystal size and position the intrinsic efficiency for this energy was calculated to be $0.9 \pm 0.1$.
<table>
<thead>
<tr>
<th>Energy (Kev)</th>
<th>Error in Fitting (%)</th>
<th>Absolute Efficiency ($\times 10^{-4}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.397</td>
<td>3.4</td>
<td>5.0 (0.3)</td>
</tr>
<tr>
<td>7.06</td>
<td>9.5</td>
<td>9.0 (1.0)</td>
</tr>
<tr>
<td>11.9</td>
<td>6.9</td>
<td>15.1 (1.4)</td>
</tr>
<tr>
<td>13.9</td>
<td>2.9</td>
<td>16.6 (1.1)</td>
</tr>
<tr>
<td>14.41</td>
<td>1.4</td>
<td>16.7 (9)</td>
</tr>
<tr>
<td>17.8</td>
<td>3.8</td>
<td>16.4 (1.2)</td>
</tr>
<tr>
<td>20.8</td>
<td>3.8</td>
<td>18.9 (1.4)</td>
</tr>
<tr>
<td>26.35</td>
<td>0.8</td>
<td>25.7 (1.7)</td>
</tr>
<tr>
<td>30.85</td>
<td>0.7</td>
<td>26.8 (1.9)</td>
</tr>
<tr>
<td>32.06</td>
<td>0.8</td>
<td>27.8 (1.7)</td>
</tr>
<tr>
<td>35.0/35.8</td>
<td>0.9</td>
<td>28.0 (2.0)</td>
</tr>
<tr>
<td>36.4</td>
<td>0.8</td>
<td>28.4 (1.8)</td>
</tr>
<tr>
<td>37.3</td>
<td>3.4</td>
<td>27.1 (2.0)</td>
</tr>
<tr>
<td>53.2</td>
<td>0.5</td>
<td>35.3 (2.5)</td>
</tr>
<tr>
<td>59.54</td>
<td>0.5</td>
<td>34.7 (1.8)</td>
</tr>
<tr>
<td>79.6/81.0</td>
<td>0.4</td>
<td>32.4 (2.3)</td>
</tr>
<tr>
<td>122.06</td>
<td>0.4</td>
<td>19.6 (9)</td>
</tr>
<tr>
<td>136.33</td>
<td>1.5</td>
<td>15.9 (9)</td>
</tr>
<tr>
<td>160.63</td>
<td>2.8</td>
<td>10.1 (0.8)</td>
</tr>
</tbody>
</table>

Absolute Efficiency = \[
\frac{\text{Peak Area}}{\text{Source Activity \times Intensity \times Time}}\]
4.2.1.2 Detection System Linearity and Resolution

The linearity of the whole detection system i.e. HpGe, electronics and MCA was assessed by recording the channel numbers for the centroids of the gamma-ray peaks in the spectrum for an unshielded $^{241}\text{Am}$ source. Plotting these channel numbers as a function gives the graph shown in Fig. 4.5, the straight line fit has a correlation coefficient of 0.99998 indicating satisfactory linearity. The system was also very stable with a change of $<0.1$ channel out of 660 for the centroid of the 59.5 KeV line over a three month period.

Detector resolution is usually defined as the full width at half maximum (FWHM) for a given peak. The manufacturers specification quoted a FWHM of 490 eV for the 122 KeV gamma-ray from $^{57}\text{Co}$ and 204 eV for the 5.9 KeV X-ray emitted by $^{55}\text{Fe}$. In practice the higher energy resolution was about $480 \pm 5$ eV but the lower energy peak generally had a FWHM in the 206-208 eV or worse. It was also found that the FWHM depended on the count rate even if this rate was low. This was demonstrated experimentally using a 370 KBq source of $^{241}\text{Am}$ with various detector collimators and spacings to achieve differing count rates, the peak widths for the 59.5 KeV line are shown as a function of count rate in Fig. 4.6, the best resolution corresponding to a width of 370 eV. It was found that the peak width at 170 counts per second (cps) was 4% greater than that at 10 cps. This effect is probably due to the pulsed optical feedback pre-amplifier fitted to the detector. It is known that for relatively high count rates (of
HpGe Detector Intrinsic Efficiency
(50 mm Source to Detector)

Fig. 4.4
Channel Number vs. Photon Energy

Peak Width (FWHM) vs. Count Rate

Fig. 4.5

Fig. 4.6
order 1000 cps) that this design suffers from a suppression of the higher energy components in a gamma-ray spectrum due to the greater probability of these events resetting the pre-amplifier (PES 80, BOD 83, FUN 83). Whatever the cause of this broadening it has important implications for fitting programs such as SAMPO that assume a fixed peak shape for a given energy and could therefore give incorrect estimates for peak areas should the count rate alter and the fitting parameters not be recalculated.

The FWHMs for Fig. 4.6 were determined by fitting Gaussian functions to the spectral peaks using the method of Mukyomo (MUK 75) in which the function is linearised. Consider a Gaussian function with a centroid $x_0$, amplitude $y_0$ and a standard deviation $\sigma$ (FWHM = 2.35 $\sigma$):

$$y(x) = y_0 \exp\left(- \frac{(x - x_0)^2}{2\sigma^2}\right) \quad (4.7)$$

If we define the quantity $Q(x)$ to be:

$$Q(x) = \frac{y(x - 1)}{y(x + 1)} \quad (4.8)$$

then:

$$\ln Q(x) = 2 \frac{(x - x_0)}{\sigma^2} \quad (4.9)$$

This is a linear function of the parameters $x_0$ and $\sigma^2$ and hence their values can be found by using standard linear least squares fitting algorithms (e.g. BEV 69). For this to be valid the correct weighting must be applied to the values of the
function \( \ln Q(x) \), and if we assume Poisson statistics then it can be shown that this uncertainty, \( \sigma_{\ln Q(x)} \) will be given by:

\[
\sigma_{\ln Q(x)}^2 = \left( \frac{1}{y(x - 1) + 1} / y(x + 1) \right)
\] (4.10)

A FORTRAN program was written to implement this fitting procedure and its effectiveness verified using artificially generated Gaussians. It was found that a Gaussian function gave a satisfactory representation of the peak shape as is shown in Fig. 4.7 though the addition of a low energy tail may improve this fit (HEL 80).

A further problem experienced was a sudden and significant increase in the detector leakage current which occurred at roughly six monthly intervals. This caused the pre-amplifier reset rate to rise from 5 per second to 50 per second. This was accompanied by a significant low energy tailing in the spectrum for \(^{55}\text{Fe} \) (5.9 & 6.4 KeV) as shown in Fig. 4.8a. Thermally cycling the detector (i.e. allowing it to warm up to room temperature and then cooling it again) restored the detector to normal operation, see Fig. 4.8b, suggesting that the problem may have been due to some contaminant in the cryostat condensing on the face of the crystal. A regular check of the pre-amplifier reset rate was necessary to ensure that any deterioration of the detector performance was identified before the high leakage could cause any damage and that no scattering spectra were recorded using the instrument in its impaired state.
Fig. 4.7 Fitting of Linearised Gaussian to 60 KeV Photopeak

Comparison of Fe-55 Spectra Before and After Thermal Cycling

Fig. 4.8
4.2.1.3 Dimensions of the Crystal

A finely collimated beam of gamma-rays was scanned across the face of the detector and down the length of the cryostat housing to determine the size and location of the crystal. This procedure was automated using the BBC microcomputer and electronics described in Chapter 5 for the tomography experiments but with the HpGe replacing the NaI(Tl) detector and the stepper motors being used to move the source across the detector face rather than moving a test object.

The initial experiment used a 1mm diameter collimator, 50 mm long, with the 7.4 Gbq $^{241}$Am source moving in 1mm steps to produce a high resolution map of the detector response to 60 KeV photons, as shown in Fig. 4.9. From this the active area corresponding to the FWHM was determined to be $170 \pm 5 \text{ mm}^2$ and the full width at tenth maximum (FWTM) to be $230 \pm 5 \text{ mm}^2$ compared with the manufacturer's estimate of $200 \text{ mm}^2$. A point worth noting is that this active area is in fact square, not circular, and thus estimates of the area relying on a single scan across the crystal and assuming this to give the diameter of a circle will be in error.

A second experiment was performed using an $^{55}$Fe source (5.9 & 6.4 KeV) to examine the low energy response of the HpGe. Unfortunately the count rate from this source was much lower than that of the $^{241}$Am and so shorter collimator, 10 mm by 1mm diameter had to be employed. To allow a realistic comparison a
Fig. 4.9 Spatial Response Of Detector Face to 60 KeV Photons (50 mm Long Collimation)
Fig. 4.10 Spatial Response Of Detector Face to 6 KeV Photons (10 mm Long Collimation)
Fig. 4.11 Spatial Response Of Detector Face to 60 KeV Photons (10 mm Long Collimation)
second 60 KeV response was also recorded using this collimator. The results are displayed in Figs. 4.10 & 4.11 and demonstrate that for 6 KeV the detector has a smaller active area than for 60 KeV (FWHM of $100 \pm 10 \text{ mm}^2$ compared to $170 \pm 10 \text{ mm}^2$). The cutoff at the edge of this active area is not as well defined for the 6 KeV as it is for the higher energy suggesting that this effect may be due to presence of a dead layer at the edges of the crystal, perhaps due to guard rings, that is thick enough to stop the lower energy photons but not to seriously attenuate the 60 KeV gamma-rays.

The depth of the crystal and its distance from the front of the housing were estimated by scanning the collimated $^{241}$Am source along the side of the cryostat. Fig. 4.12 shows how the count rate varied with position. It would appear that the active depth extends from 6 mm to 16 mm behind the detector window but that the front section of the crystal is partly obscured - perhaps by the guard rings already postulated. This result is in agreement with the manufacturer's specification which states the active volume to be 10 mm deep.

An alternative way of estimating the "effective" distance between the crystal and the front window of the detector is to use the inverse square law (POT 84). If $x$ is this distance then the count rate for a source at a position $d$ from the front face of the detector will be:

$$\text{count rate} = \text{constant} / (x + d)^2 \quad (4.11)$$
Count Rate vs. Distance

Square Root of Count Rate vs. Distance

Fig. 4.12

Fig. 4.13
Thus by plotting the inverse square root of the count rate as a function of distance it is possible to find \( x \).

Providing the energy of the photons used is sufficient to ionise the full depth of the crystal this distance \( x \) will correspond to the centre line of the active volume (POT 84). Fig. 4.13 shows the results obtained for an \(^{241}\)Am source; extrapolating the fitted line gives the centre of the active volume as \( 11.0 \pm 0.5 \) mm behind the detector face in agreement with the results of the linear scan.

4.2.2 Radionuclide Sources

There are several factors that limit the choice of gamma-ray source for coherent scattering experiments. In order to have a measureable elastic scattering signal from bone it is necessary to have a photon energy less than or equal to about 100 KeV, as the coherent cross-section drops dramatically for higher energies. To give adequate penetration of osseous tissue there is a lower energy limit of about 20 to 30 KeV. As the ultimate aim would be a system for medical use any sources used must be available with sufficiently high photon fluxes to keep the measurement times reasonably short. It is also an advantage to have no extraneous gamma- or X-rays present in the photon spectrum that would only contribute to the dose without providing any information on bone status.

The majority of the experiments presented here were done using an \(^{241}\)Am source with an activity of 18.5 Gbq. The decay
scheme for this nuclide is shown in Fig. 4.14, its emission spectrum being mainly the 59.54 KeV gamm-ray (CAM 86) and the associated neptunium L X-rays, ranging from 12 to 22 KeV. These latter energies are almost totally absorbed by the steel source encapsulation giving, effectively, a mono-energetic photon source as can be seen in Fig. 4.15. $^{241}$Am has been widely used in coherent to Compton scattering ratio experiments (PUU 76, LIN 82, KAR 83, LEI 84, GIG 85b, SHU 86 & 87, HAR 87) due to its almost ideal gamma-ray spectrum and also its ready availability and long half-life (432.9 years - BAR 84). Unfortunately this slow decay rate and the high degree of self-absorption within the americium itself, due to its high atomic number (Z=95), limit the flux available. Karellas et al (KAR 83) built a line source using six 7.4 GBq beads of $^{241}$Am to give an approximate photon output of $3.3 \times 10^8$ photons per second per steradian. This was sufficient to carry out clinical trials with a measurement time of about fifteen minutes (SHU 86 & 87). In contrast the source used for this work was in the form of an extended disc, diameter 18 mm, thus reducing the self absorption and giving a flux of order $2.8 \times 10^8$ photons /s /sr. This is the manufacturer's figure but was verified experimentally.

A few experiments were done using a borrowed $^{153}$Gd bead source, its decay scheme and measured gamma-ray spectrum are shown in Figs. 4.16 & 4.17. The lines of interest are at 97.4 and 103.2 KeV (LED 78) but there are also other, lower intensity, gamma-rays and europium K X-rays, 41 to 48 KeV, present and these are not easily filtered out. The half-life for
Fig. 4.14 Decay Scheme of Am-241 (From SOW 83)

Fig. 4.15 Spectrum From Am-241 Source
Fig. 4.16 Decay Scheme of Gd-153 (From SOW 83)

Fig. 4.17 Spectrum From Gd-153 Source
$^{153}$Gd is 242 days (LED 78) and as the source was two years old it had decayed from its original, nominal, activity of 3.7 GBq to 440 MBq and its photon flux for the 97 & 103 KeV gamma-rays was measured to be $2 \times 10^7$ photons /s /sr. It was necessary to use long collection times to acquire an adequate number of counts but using information supplied by the manufacturer on the photon flux that could be obtained from a new 35 GBq source ($7.5 \times 10^8$ photons /s /sr) it was possible to scale the measurements to those that would be achieved on a clinical system, in an acceptable time.

4.2.3 Volume of Interaction

The collimators used in these experiments were all simple cylindrical or rectangular bores. Some attempts were made to use bunches of tantalum tubes to define a beam with a small divergence, following the example of Webber and Kennett (WEB 76) and of Kerr et al (KER 80), but the count rate for such an arrangement was too low for practical purposes.

As can be seen in Fig. 4.2 some of the collimators were made of brass which has a mean free path for 60 KeV photons of approximately 0.7 mm (the exact figure depends on the composition of the alloy employed). There was a possibility that septal penetration could occur and so the shape of the photon dispersion from the collimators was checked using X-ray film exposed for approximately 12 hours and, after development, examined using a photo-densitometer. The size of the darkened
area on the films as function of distance was consistent with the cone defined by the bore of the collimators, indicating that no significant gamma-ray flux was penetrating the edges of the brass.

The volume of interest in these scattering experiments is that which is viewed by both source and detector collimators i.e. the intersection of the cones, or pyramids, defined by these collimators. The maximum linear dimensions of this shape (the longest diagonal) can be calculated quite readily but its volume is much harder to determine due to the complicated form of the intersection. A numerical method, based on the work of Balogun (BAL 86), was used to estimate this volume; a small volume element is stepped through the region defined by the first collimator and if it also lies within the limits of the second one then the volume is incremented by one volume element. The element size is decreased until subsequent iterations agree within a pre-determined limit, a value of 1% being chosen for these calculations. This procedure was not guaranteed to give a true figure and it was found necessary to estimate the volume at angles close to the one of interest to ensure that consistent and valid results were obtained.

For cylindrical bore collimators as depicted in Fig. 4.18 the volume of interest within the first cone can be defined as:
\[
\int_{z_{\text{min}}}^{z_{\text{max}}} \int_{z \tan a}^{z \tan a'} \left( \sqrt{z^2 \tan^2 a - y^2} - \sqrt{z^2 \tan^2 a' - y^2} \right) \, dy \, dx
\]

(4.12)

where \(z_{\text{max}}\) and \(z_{\text{min}}\) are the maximum and minimum extents, in the \(z\) direction, of the region ACEG. That is the maximum and minimum of the \(z\) co-ordinates for the points \(A, C, E\) and \(G\) given by:

\[
A_z \text{ or } C_z = J_1 + K_1 \left( \cos \theta - \sin \theta \cot(\theta - b) \right) \frac{1 \pm \tan a \cot(\theta - b)}{}
\]

(4.13)

\[
E_z \text{ or } G_z = J_1 + K_1 \left( \cos \theta - \sin \theta \cot(\theta + b) \right) \frac{1 \pm \tan a \cot(\theta - b)}{}
\]

(4.14)

The condition for any point, \(P\), within this volume also lying within the cone defined by the collimator is that the line \(PK\) should be at an angle less than or equal to \(b\) to the line IK.

For a collimator with a rectangular cross-section oriented such that it defines a pyramid of half angle \(a\) in the horizontal plane and a half angle \(a'\) in the vertical plane, then equation 4.12 becomes:

\[
\int_{z_{\text{min}}}^{z_{\text{max}}} \int_{z \tan a}^{z \tan a'} \int_{z \tan a}^{z \tan a'} \left( \sqrt{z^2 \tan^2 a - y^2} - \sqrt{z^2 \tan^2 a' - y^2} \right) \, dy \, dx
\]

(4.15)

Similarly for such a collimator centred on the point \(K\) in
Fig. 4.18 Region of intersection for two collimators
Fig 4.19
EFFECT OF SCATTERING ANGLE ON VOLUME OF INTERSECTION
Fig. 4.20 Variation of Scattered Count Rate with Position Within the Scattering Volume. The 500 contour line corresponds to approx. 75% of the maximum.
Fig. 4.18 with half angles $b$ and $b'$, a point, $P$, will be in the interaction volume if the horizontal and vertical projections of the line $PK$ lie within these angles.

This algorithm was coded in a FORTRAN program and implemented on the University of Surrey Prime computers.

The shape of the scattering volume becomes significantly elongated for small angles, as can be seen in Fig. 4.19, but the extremities of this region will not contribute as much to the overall scattering as the central region as the solid angle subtended by the detector or source is smaller at these points. This is demonstrated experimentally by Fig. 4.20 which shows how the scattered gamma-rays, both elastic and inelastic summed together, from a 0.7 mm diameter copper wire varied with position within the region defined by two 50 mm long collimators with 8x5 mm$^2$ cross-sections. The source used was the 18.5 GBq of $^{241}$Am with a NaI(Tl) detector, the scanning being done with stepper motors under computer control as before.

4.2.4 Peak Area Estimation and Peak Fitting

For the scattered gamma-ray spectra for $^{241}$Am at angles greater than about 50 degrees the separation of the coherent and Compton peaks is sufficient for the simple area estimation routine provided on the MCA to be used. The user defines a region of interest (ROI) around the peak of interest and the MCA then displays the total number of counts in this region, the integral,
and also the number remaining after the subtraction of a simple trapezium background, defined by the average counts in the first and last four channels of the ROI. The error in this quantity, taken to be the peak area, was assumed to be:

\[ \sigma_{\text{area}} = \sqrt{2 \cdot \text{integral} - \text{area}} \]  

Unfortunately small scattering angles for both the sources used gave spectra with considerable degrees of overlap between the peaks with the coherent peak lying on the high energy tail of the Compton line-shape as shown in Fig. 4.21. It was felt that the simple straight line interpolation provided by the MCA would not accurately represent the background under the elastic peak and that some form of peak fitting ought to be used. The modified SAMPO package (CAR 77, ROU 69) used to determine the peak areas for the efficiency measurements was not considered suitable (KER 85, McC 85) as it requires an a priori calibration of peak width and tailing parameters and it has been shown that the width varies with count rate for this detector. It also assumes a quadratic background under the fitted peaks and this was found to be an inadequate description of the shape of the Compton tail underlying the coherent peak for some situations. Thus a small suite of FORTRAN programs was specially written to provide a method of peak fitting for this particular situation.

There are a number of peak fitting programs discussed in the literature (e.g. ROU 69, McN 75, KOS 81, HEL 83) and the
Counts

XI0^3 30 Degree Scattering - Am-241

Compton

Coherent

Fig. 4.21
shape chosen for the detector response function (i.e. the peak shape for mono-energetic photons) is usually a Gaussian with some form of additional tailing function or functions (JOR 77, CAM 79). It has been pointed out (HEL 80) that while increasing the number of parameters will lead to an improvement in the fitting some of the subsidiary functions have little physical significance and that as simple a function as possible is probably the best approach (PRU 82). A simple Gaussian was therefore chosen to represent the coherent peak shape in this instance.

The form of the background under this Gaussian depends on the scattering angle. Following the example of SAMPO a simple polynomial was tried as a method of interpolating between the points either side of the peak, but a quadratic was the highest order that could be used without physically unrealistic oscillations appearing in the shape of the fitted background. This gave an overall fitting function, \( y \), for channel number \( x \) of the form:

\[
y(x) = A \exp\left(-\frac{(x-B)^2}{2C^2}\right) + D + Ex + Fx^2
\]  

(4.17)

where \( A \) to \( F \) are the parameters to be found. This function proved suitable to describe the 97 KeV coherent scattering peak in the \(^{153}\text{Gd} \) experiments as shown by the example in Fig. 4.22.

An alternative form that was used to represent the shape of the higher energy limit of the Compton peak was an exponential
Fig. 4.22 Gaussian plus Quadratic Functions Fitted to Scattering Spectrum
Fig. 4.23 Gaussian plus Exponential Functions Fitted to Scattering Spectrum
Fig. 4.24 Two Gaussian Functions Fitted to Scattering Spectrum
function:

$$y(x) = A \exp\left(-\frac{(x-B)^2}{2C^2}\right) + D + E \exp(-Fx) \quad (4.18)$$

Fig. 4.23 shows an example of this function fitted to the 103 KeV coherent peak in a $^{153}$Gd scattering spectrum.

In the case of small angle scattering where the coherent and Compton peaks are overlapping to some degree two Gaussians are used to represent the data:

$$y(x) = A \exp\left(-\frac{(x-B)^2}{2C^2}\right) + D + E \exp\left(-\frac{(x-F)^2}{2G^2}\right) \quad (4.19)$$

Rigorously the shape of the Compton peak will be given by the response function of the detector folded with the range of energies corresponding to the angular acceptance of the collimators, but in practice it was found that the high energy side of the inelastic peak could be adequately described by a Gaussian line-shape, an approximation often adopted in measurements of elastic cross-sections (KAN 87). An example of this function fitted to a 30 degree scattered spectrum from $^{241}$Am is shown in Fig. 2.24.

The values for the fitting parameters are found by locating the minimum for the quantity $\chi^2$ (Chi-squared) defined as (BEV 69):

$$\chi^2 = \sum_x \left( y_{\text{data}}(x) - y_{\text{fit}}(x) \right)^2 / \sigma^2(x) \quad (4.20)$$
where \( \sigma^2(x) \) is the uncertainty in the \( x^{th} \) value. Assuming Poisson statistics this will be:

\[
\sigma^2(x) = y_{\text{data}}(x)
\]  

(4.21)

When the function being used has a linear dependence on its parameters then it is possible to find an analytical solution for this minimisation, but for the functions in equations 4.17-19 non-linear methods have to be adopted. An initial attempt used a simple iterative search (MOS 87) but this was computationally inefficient and a non-linear minimisation algorithm available as a sub-routine in the NAG library on the Surrey computers was finally adopted. It was necessary to provide an initial estimate of the parameters but the routine then rapidly converged to a minimum, with a subsequent checking routine to ensure that it had not located a subsidiary minimum rather than the main one. Graphical output, as already shown above, was produced showing the overall fit and the shape of the background function. A second graph displaying the differences between the data and fitted function in terms of the number of standard deviations (i.e. \( \sqrt{y} \)) was also given. If the function being used was a good representation of the spectrum then these residuals would have a random distribution largely within the range from -2 to +2, any systematic pattern or excessively large values would indicate that the model chosen was not a good description of true data.

A measure of the quality of the fitting to a given
function is provided by the reduced Chi-squared, \( \chi^2_r \), defined as (BEV 69):

\[
\chi^2_r = \frac{\chi^2}{\text{No. of Degrees of Freedom}} \quad (4.22)
\]

where the number of degrees of freedom is the number of data points less the number of parameters. A good fit will yield a value for the reduced Chi-squared of approximately unity, larger values indicating a poorer fit.

The area of the peak was taken to be the area of the fitted Gaussian, the associated error (one standard deviation) being given by:

\[
\sigma^2_{\text{Area}} = \begin{cases} 
(Area + 2.\text{Background}) \chi^2_r & \text{for } \chi^2_r > 1 \\
(Area + 2.\text{Background}) & \text{for } \chi^2_r < 1
\end{cases} \quad (4.23)
\]

where the background is the area of the function underlying the Gaussian peak.

A set of artificial spectra, which had a normally distributed noise component added, were used to verify the correct operation of these programs and the accuracy of the fitted parameters. In general use, with real spectra, it was found necessary to spend a little time optimising the region of interest for the various scattering angles using the graphical output and reduced Chi-squared. Once the best ROI had been established, i.e. the one that gave the lowest \( \chi^2_r \), it was found
consistent for all the spectra of that given form.

For those scattering angles where the coherent and Compton peaks were not well separated (overlapped) the total area for both was estimated using the trapezium subtraction method discussed above and the inelastic peak area found by taking away from this the area found by the fitting programs for the coherent peak. All the errors were added in quadrature to find the estimated uncertainty in these values.

4.3 Optimisation of the Scattering Angle

The choice of scattering angle depends on several factors. The differential cross-sections for coherent and, to a lesser extent, Compton scattering are forward peaked and thus smaller scattering angles will give higher count rates. This is, however, at the expense of peak separation as the Compton energy shift is reduced. These effects can be seen in Fig. 4.25 which shows the photon scattering spectra collected at various angles for a simple calcium carbonate and wax phantom (84% & 16% by weight, respectively) irradiated with the $^{241}$Am source. The collection time was 60 000 s for all but the 90 degree scattering when 120 000 s was used. It is apparent that for the latter case the coherent peak is poorly defined against the background noise, though it is for this angle that the scattering volume has its most regular shape (Fig. 4.19). As discussed in section 2.7.3 the sensitivity (i.e. relative change in differential cross-section for a given change in the scattering material) is greater at
these angles than at the smaller ones.

This section considers the problem of the optimum angle for $^{241}$Am, the case for $^{153}$Gd is discussed in section 4.5.

4.3.1 Calculations

When considering this problem quasi-theoretically for the coherent to Compton ratio technique Karellas et al (KAR 83) assumed a simple parameterisation of the form $Z^{n-1}$ for this ratio and demonstrated that the value of his exponent increased with angle thus indicating increased sensitivity for larger angles. Rather than rely on such assumptions an alternative approach was adopted using the program already discussed in section 3.2.2 to calculate the coefficients $u_{coh}(\theta)$ and $u_{incoh}(\theta)$ directly. This was done for $K_2HPO_4$ solutions, using the experimentally determined densities, and for mixtures of yellow marrow and cortical bone, as defined by Woodard and White (WOO 82), to model the spongiosa of distal sites in the adult skeleton. These coefficients are shown as functions of density or bone mineral concentration (BMC), as appropriate, in Figs. 4.26-29, and have been normalised to the values for water or pure marrow to allow comparison between the different angles. It can be seen that for trabecular bone $u_{coh}$ is linearly dependent on BMC as would be expected from the mixture rule (eqn. 3.8). It will also be noted that the coherent to Compton ratios, when plotted as functions of solution density or BMC, are not perfectly straight lines.
Fig. 4.25 Scattering Spectra at Various Angles from CaCO3/wax
Fig. 4.26 \( n_{coh} \) versus density for K2HPO4 solution

Fig. 4.27 \( R_{cc} \) versus density for K2HPO4 solution
Normalised muh coherent vs. BMC

Fig. 4.28 $u_{coh}$ versus BMC for trabecular bone

Normalised coh/Compt

Fig. 4.29 $R_{cc}$ versus BMC for trabecular bone
The slopes of these normalised curves give a measure of the sensitivity, a steeper line giving a greater relative change in the coherent peak area or coherent to Compton ratio ($R_{cc}$) for a given change in density or BMC. These slopes are plotted as functions of angle in Figs. 4.30-33 and it can be seen that the results are in keeping with those of Karellas et al (KAR 83) indicating that the greatest sensitivity for $R_{cc}$ is for the larger angles, but there is also an increase in the sensitivity for angles below 40 degrees. The graph for the coherent scattering alone displays the same form indicating that it is the variation in the elastic cross-section that has the greatest influence on the ratio $R_{cc}$. To include the effect of the counting statistics that would limit the accuracy of a real measurement these curves were weighted by a factor of $\sqrt{u_{coh}(\theta)}$ and are displayed on the same graphs. It can be seen that the increase in inherent sensitivity for larger angles is more or less balanced by the poorer count rate and for both scattering methods the smaller angles have slightly better overall sensitivity.

While providing a useful indication of the angular dependence of the sensitivity the above calculations do not take account of all the factors that are to be found in a real experiment, such as the increase in the attenuation of the photon beams with increasing density of the scattering material and the finite range of angles accepted through the collimators.
Sensitivity of muh coherent vs. angle

![Graph](Image)

Fig. 4.30 $u_{coh}$ sensitivity versus angle for K2HP04 solution

Sensitivity coh/compt vs. angle

![Graph](Image)

Fig. 4.31 $R_{cc}$ sensitivity versus angle for K2HP04 solution
Sensitivity of muh coherent vs. angle

Fig. 4.32 \( u_{coh} \) sensitivity versus angle for trabecular bone

Sensitivity of coh/Compt vs. Angle

Fig. 4.33 \( R_{cc} \) sensitivity versus angle for trabecular bone
4.3.2 Experimental Optimisation of the Scattering Angle

To establish the best angle experimentally the apparatus shown schematically in Fig. 4.2 was used. The source holder was fixed on the end of a rotating arm with its pivot on the centre line of the detector collimator to ensure correct alignment of the system. Over this centre of rotation was a small table with a piece of polar graph paper stuck on it to allow accurate positioning and centring of the samples (better than 0.5 mm). Some of these features can be seen in Fig. 4.45. Solutions of $K_2HPO_4$ with relative densities from 1.0 to 1.7, stored in 50 mm diameter polythene bottles, were used to represent bone. Scattering spectra were collected at angles ranging from 30 to 90 degrees in 10 degree steps and Table 4.3 displays the calculated volumes and maximum linear dimensions for each position. The collimators used were 50 mm long with a rectangular cross-section, 8 mm x 5 mm, with the shorter side parallel to the scattering plane, and this gave an angular dispersion of ±11 degrees about the central angle. Even for the smallest angle the interaction volume was completely contained within the sample.

The photon flux available through the source collimator was measured as $6 \times 10^5$ gamma-rays s$^{-1}$ in agreement with that expected from simple calculations. This rather low output meant that long acquisition times were needed to achieve adequate counting statistics for the larger scattering angles. A collection time of 86400 s (24 hours) was used for all the measurements. The coherent peak area for the solution with
relative density 1.68 is displayed in Table 4.3 for each angle to show the variation in count rate.

As the phantoms used were symmetrical it was not necessary to take two separate scattering measurements to determine the coherent to transmission ratio, $R_{ct}$ (eqn. 4.5), one spectrum being equivalent to the two separate measurements assuming that the total collection times remained the same. Lack of equipment meant that the transmission measurements could not be done simultaneously with the scattering, as would be required by dose and time considerations in a clinical system, but had to be carried out separately using the HpGe in the 0 degree position with a brass plate acting as a filter to keep the system dead time below 5%. In a clinical instrument the second detector would probably be a cheap, low resolution, detector such as a sodium iodide scintillation counter and not a second HpGe.

All the scattering spectra were analysed using the fitting programs described in section 4.2.4 the average values for the reduced Chi-squared are given in Table 4.4. The coherent to Compton ($R_{cc}$) and coherent to transmission ($R_{ct}$) ratios were calculated and normalised to the values for water to allow comparisons to be made between the different angles. The results are displayed in Figs. 4.34-40 plotted as a function of the solution density. A weighted linear least squares fit was used to fit the curves shown, a straight line gave an adequate description of $R_{cc}$ but a quadratic function was needed for $R_{ct}$ to account for the curvature. Following Karellas et al
Fig 4.34
Rct and Rcc (normalised to water) versus K2HP04 Solution Density

Fig 4.35
Rct and Rcc (normalised to water) versus K2HP04 Solution Density
Fig. 4.37
Rct and Rcc (normalised to water)
versus K2HPO4 Solution Density

Fig. 4.36
Rct and Rcc (normalised to water)
versus K2HPO4 Solution Density
Fig 4.40

Rct and Rcc (normalised to water) versus K2HP04 Solution Density

\[ \text{Relative Density} \]
(KAR 83) the sensitivity for a given angle can be defined in terms of the uncertainty in the measured density, \( dp \), given by:

\[
dp = \frac{dR}{S} \tag{4.23}
\]

where \( dR \) is the uncertainty in the ratio, \( R_{ct} \) or \( R_{cc} \), and \( S \) is the slope of the ratio versus density curve. In this work these errors were taken to be one standard deviation (1 s.d.). The values for \( dp \) were calculated and the results are given in Table 4.4. and are quoted in units of Kg m\(^{-3}\) assuming the density of water to be 1000 Kg m\(^{-3}\).

It can be seen that for a given angle \( R_{ct} \) has a lower uncertainty than does \( R_{cc} \) indicating higher sensitivity. The variation of sensitivity with angle for both ratios is such that smaller angles have the lowest statistical error, in agreement with the calculations.

The counting time used in this experiment was clearly unacceptable for use in a clinical context, and so the collimation for both the source and detector was opened up to try to increase the count rate; Fig. 4.41 shows the apparatus used. The photon flux available in this case was estimated to be \( 3 \times 10^6 \) gamma-rays s\(^{-1} \) allowing adequate counting statistics to be collected in 2000 s (30 mins.). Unfortunately the smallest acceptable angle of scattering possible consistent with a reasonably small volume of interaction was about 70 degrees. Figs. 4.42&43 show \( R_{cc} \) and \( R_{ct} \), again normalised to the
Fig. 4.41 Scattering Apparatus
### Table 4.3 Dimensions of Scattering Volume

<table>
<thead>
<tr>
<th>Angle (Degrees)</th>
<th>Volume $(10^3 \text{ mm}^3)$</th>
<th>Max. Linear Dimension (mm)</th>
<th>Coherent Counts For Solution R.D. 1.68</th>
</tr>
</thead>
<tbody>
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<td>30</td>
<td>3.82</td>
<td>42</td>
<td>74 000</td>
</tr>
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<td>50</td>
<td>2.61</td>
<td>26</td>
<td>9 600</td>
</tr>
<tr>
<td>60</td>
<td>2.34</td>
<td>22</td>
<td>4 700</td>
</tr>
<tr>
<td>70</td>
<td>2.18</td>
<td>19</td>
<td>2 800</td>
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<td>17</td>
<td>1 900</td>
</tr>
<tr>
<td>90</td>
<td>2.07</td>
<td>16</td>
<td>1 400</td>
</tr>
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</table>

### Table 4.4 Precision in Density Determination

<table>
<thead>
<tr>
<th>Angle (Degrees)</th>
<th>Reduced Chi-squared</th>
<th>Reduced $\rho_p \text{ (Kg m}^{-3}\text{)}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$\rho_{cc}$</td>
</tr>
<tr>
<td>30</td>
<td>1.2</td>
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<td>2.5</td>
<td>12</td>
</tr>
<tr>
<td>50</td>
<td>1.9</td>
<td>17</td>
</tr>
<tr>
<td>60</td>
<td>1.4</td>
<td>21</td>
</tr>
<tr>
<td>70</td>
<td>1.2</td>
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<td>1.1</td>
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<tr>
<td>90</td>
<td>0.9</td>
<td>23</td>
</tr>
</tbody>
</table>

Uncertainties in $\rho_p$ estimated to be about $\pm 10\%$
Table 4.5 Dimensions for Scattering Volume and Precision of Density Measurements for Wide Collimation

<table>
<thead>
<tr>
<th>Angle (Degrees)</th>
<th>Volume $(x10^{-3} \text{ mm}^3)$</th>
<th>Max. Linear Dimension (mm)</th>
<th>Coherent Counts for Solution R.D. 1.68</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>20</td>
<td>52</td>
<td>4900</td>
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<td>90</td>
<td>19</td>
<td>43</td>
<td>2700</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Angle (Degrees)</th>
<th>$dp$ $(\text{Kg m}^{-3})$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$R_{cc}$</td>
</tr>
<tr>
<td>70</td>
<td>12</td>
</tr>
<tr>
<td>90</td>
<td>14</td>
</tr>
</tbody>
</table>

Uncertainties in $dp$ are estimated to be about ± 10%
Rct & Rcc (Normalised) for 70 Degrees

Scattering Ratio

Relative Density

○ Rct  ▲ Rcc

Fig. 4.42

Rct & Rcc (Normalised) for 90 Degrees

Scattering Ratio

Relative Density

○ Rct  ▲ Rcc

Fig. 4.43
value for water, for 70 and 90 degree scattering with this collimation. As the gamma-ray peaks were well separated the trapezoidal background subtraction facility on the MCA was used to estimate the peak areas. The estimated statistical precisions (dp) are given in Table 4.5, where it can be seen that the smaller angle is again to be favoured and that $R_{ct}$ gives the greater sensitivity.

4.3.3 Conclusion

The experimental results indicate that for $K_2HPO_4$ solutions, and thus probably for bone, the use of separate transmission measurements to correct the coherent scattering signal for the effects of beam attenuation has a higher sensitivity for density estimation than does the ratio of coherent to Compton scattering. This verifies the assertion of Kerr et al (KER 80).

Regarding the optimum angle to employ with either technique it would appear that the need for good counting statistics was the most significant factor. For larger scattering angles the differential cross-section is more sensitive to changes in density but its magnitude is much less and thus the smaller angles are to be preferred. This is contrary to the findings of Karellas et al (KAR 83) but it should be noted that all subsequent work done by this group has quoted an angle of scattering of 71 degrees (e.g. SHU 85) which is consistent with the lowest angle possible with the wide beam.
Smaller angles of scattering require tightly collimated beams to keep the interaction volume within the dimensions of a trabecular bone site, and for $^{241}$Am sources, limited by their high degree of self-absorption, this reduces the photon output too drastically for practical use. Radionuclides with a higher photon output such as $^{153}$Sm as used by Kerr et al (KER 80) or $^{153}$Gd as employed by Stalp and Mazess (STA 80) can be used at smaller scattering angles and some work with the latter source is presented in section 4.5.

4.4 Precision and Sources of Error

4.4.1 Experimental Arrangement

The apparatus and geometry finally adopted for these scattering measurements is shown in Figs. 4.44&45, the scattering angle being 70 degrees as determined in section 4.3. As before the transmission measurements were done separately using the HpGe and a 1 mm thick brass plate, placed between the object and the detector, to keep the dead time below 3%, a collection time of 300 s was sufficient to achieve good statistics. The volume of interaction was $6.1 \times 10^{-3} \text{ mm}^3$ with a maximum linear dimension of 35 mm. The photon output available through the source collimator is $3 \times 10^6$ gamma-rays s$^{-1}$, and this allows a coherently scattered peak of $7 \times 10^3$ counts to be collected in 10 000 s (2.8 hrs.) for a $\text{K}_2\text{HPO}_4$ solution with
Fig. 4.45 Photographs of the gamma-ray scattering apparatus.
70 Degree Scattering Am-241

Counts

Fig. 4.46
This has to be compared with the apparatus used by Leichter et al (SHU 85, LEI 85) which could acquire the same number of counts in approximately 1 000 s, for an estimated dose of 3 mGy. The significant difference in measurement time is due to the sources being used; the diffuse 18.5 GBq source available at Surrey had to be 215 mm from the centre of the scattering volume to minimise beam divergence whereas the 44 GBq line source used by the Californian group was placed only 110 mm away. This line source has been used in a practical clinical instrument by Shukla et al (SHU 86).

The angle chosen is large enough to give good separation of the two scattering peaks as can be seen in Fig. 4.46 which shows a typical spectrum. Thus it is possible to use the built in area function on the MCA to estimate the counts in each peak, the ROI being selected to correspond to three standard deviations either side of the centroid.

4.4.2 Bone Phantoms

Using the standard $K_2HPO_4$ phantoms with relative densities from 1.0 to 1.7, placed in 40 mm diameter bottles for this occasion, the graph shown in Fig. 4.47 was produced. The estimated precision for $R_{cc}$ was 8.2 Kg m$^{-3}$ whereas for $R_{ct}$ it was 3.5 Kg m$^{-3}$. To represent more closely the density range of trabecular bone and to give a greater number of data points the
Rct & Rcc (Normalised) for 70 Degrees

Scattering Ratio

Relative Density

○ Rct ▼ Rcc

Fig. 4.47
BL1 to 11 series of $K_2HPO_4$ phantoms with relative densities from 1.0 to 1.4 was used to produce the curves displayed in Figs. 4.48 & 49. With this reduced density range both curves could be adequately described by straight lines. The statistical precisions attainable in this case were estimated to be 5.3 Kg m$^{-3}$ for $R_{cc}$ and 4.8 Kg m$^{-3}$ for $R_{ct}$. It would appear that the advantage in the latter is not as significant for lower densities as it was for solutions with relative densities up to 1.7. This is consistent with the dependence of the elastic scattering cross-sections on atomic number (roughly $Z^n$) which will give $R_{ct}$ greater sensitivity when more of the high atomic number elements are present.

The PEPHA & GB phantoms were designed to give a close representation of spongiosa and the results of scattering measurements can be seen in Figs. 4.50 & 51. It is apparent that the different phantoms give significantly different values of $R_{ct}$ and $R_{cc}$ for the same BMC. This is a result of the differences in scattering cross-sections between the MSG and petrolatum used to represent the bone marrow, as discussed in chapter 3. This highlights the need for suitable bone phantoms to calibrate bone densitometry equipment. It also shows the influence that variations in marrow composition will have on estimates of BMC, though it is believed that for an adult the spongiosa of distal sites such as the os calcis contains only yellow marrow (CRI 81). In this case the curve for true trabecular bone would lie between the two extremes shown as petrolatum has a smaller cross-section than yellow marrow and
the MSG base material of the GB phantoms has a larger one.

The precisions achieved were 3.5 Kg m\(^{-3}\) (R\(_{cc}\)) and 3.4 Kg m\(^{-3}\) (R\(_{ct}\)) for the PEPHA phantoms and 6.1 Kg m\(^{-3}\) (R\(_{cc}\)) and 5.5 Kg m\(^{-3}\) (R\(_{ct}\)) for the GB phantoms. Again the improvement in sensitivity arising from the use of transmission measurements is not as marked as it is for the denser solutions of K\(_2\)HPO\(_4\).

### 4.4.3 Influence of Sample Size

Increasing the size of the samples used will increase the degree of multiple scattering present in the measured spectra (KEN 76) and for the coherent to Compton ratio there will be effects due to the differential attenuation of the two scattered components, the inelastic one having a lower energy and therefore experiencing greater absorption in surrounding materials. Ling et al (LIN 82) reported that increasing the size of K\(_2\)HPO\(_4\) solution, relative density 1.5, from a cube with sides 15 mm long to one with sides of 24 mm had no significant effect on R\(_{cc}\) with 3% uncertainty in counting statistics. Hardie-Brown et al (HAR 87) also found no significant change in R\(_{cc}\) for samples of aluminium and epoxy-resin based phantoms with linear dimensions up to 50 mm, though they did not quote the statistical limits of their measurements.

To investigate the influence of size on both R\(_{cc}\) and R\(_{ct}\) measurements were made of the K\(_2\)HPO\(_4\) phantoms in both
Effect of size on $R_{cc}$

Scattering Ratio $R_{cc}$

<table>
<thead>
<tr>
<th>Relative Density</th>
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<th>1.2</th>
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<th>1.5</th>
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<tbody>
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<td>40 mm Diameter</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 4.52

Effect of size on $R_{ct}$

Scattering Ratio $R_{ct}$

<table>
<thead>
<tr>
<th>Relative Density</th>
<th>0.9</th>
<th>1</th>
<th>1.1</th>
<th>1.2</th>
<th>1.3</th>
<th>1.4</th>
<th>1.5</th>
<th>1.6</th>
<th>1.7</th>
<th>1.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 mm Diameter</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40 mm Diameter</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 4.53
Differences due to change in size

Fig. 4.54

Fig. 4.55
40 mm and 50 mm diameter bottles. The collection time was again 10 000 s. Figs. 4.52&53 show the results while Figs.4.54&55 display the differences between the two sizes in terms of the number of standard deviations (of the 40 mm samples) and as the resulting error in density determination, respectively. Assuming a normal distribution for these errors (i.e. 95% within 1.96 s.d. of the mean) then significant deviations are only apparent for solution densities greater than 1.6 and then both scattering techniques are affected. However in terms of error in density estimation it is worse for \( R_{cc} \) (up to 75 Kg m\(^{-3}\) or 4.5%) than for \( R_{ct} \) (25 Kg m\(^{-3}\) or 1.5%).

These results are in agreement with those reported for other workers in that for the densities and compositions typical of spongiosa any differences induced by changes in sample size will be less than the statistical precision of the measurements for \( R_{cc} \). Under these conditions it would appear that \( R_{ct} \) is also independent of the sample size.

4.4.4 Influence of Overlying Material

Ling et al (LIN 82) explored the effects of overlying material on coherent to Compton ratio measurements and concluded that soft tissue thicknesses greater than about 20 mm caused significant changes in the results but that the cortical bone sheath, represented in their experiment by aluminium, did not.

The constraints on the scattering geometry mean that it
is not possible to make measurements on sites covered by thick layers of soft tissue without the volume of interest becoming too large. But it was considered important to study the possible influence of overlying cortical bone on coherent scattering. Experiments were conducted using an aluminium tube, internal diameter 41.2 mm, placed around the bone phantoms to simulate compact bone. The wall thickness of this tube was 1.60 ± 0.05 mm and thus had a linear attenuation coefficient equivalent to 2.00 mm of cortical bone, consistent with the models of Woodard and White (WOO 82). Figs. 4.56-61 show the effects this aluminium had on $R_{ct}$ and $R_{cc}$ for the various bone phantoms and Table 4.6 gives the linear least squares fits for these graphs. It can be seen that the presence of the aluminium causes an increase in the measured values of both $R_{cc}$ and $R_{ct}$ though this is only of the order of 1 to 2 standard deviations and thus for any one single measurement it will not be significant.

These results indicate that there is no significant advantage in using transmission measurements to correct for beam absorption of the coherent scattering rather than using the coherent to Compton ratio despite the differential attenuation of these two energies (approximately 1% in this case). This suggests that by taking the ratio $R_{cc}$ a partial cancellation of the multiple scattering is made, as suggested by Stalp and Mazess (STA 80) which offsets the differences in attenuation. Fig 4.62 shows the scattering spectrum collected with no phantom present i.e. the gamma-rays scattered by air and the multiple scattering from the apparatus and that acquired when the aluminium tube
Table 4.6 Influence of Aluminium Tube on Scattering:

<table>
<thead>
<tr>
<th>Phantom</th>
<th>Slope</th>
<th>Intercept</th>
<th>( r^* )</th>
<th>Mean Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(m(^3) Kg(^{-1}))</td>
<td></td>
<td></td>
<td>(Kg m(^{-3}))</td>
</tr>
<tr>
<td>( \text{K}_2\text{HPO}_4 )</td>
<td>0.0839(11)</td>
<td>-0.0645(12)</td>
<td>0.9993</td>
<td>9.6</td>
</tr>
<tr>
<td>( \text{K}_2\text{HPO}_4 + \text{Al} )</td>
<td>0.0888(13)</td>
<td>-0.0691(14)</td>
<td>0.9986</td>
<td></td>
</tr>
<tr>
<td>PEPHA</td>
<td>7.84(13)x10(^{-5})</td>
<td>0.00389(15)</td>
<td>0.99998</td>
<td>5.8</td>
</tr>
<tr>
<td>PEPHA + Al</td>
<td>8.05(15)x10(^{-5})</td>
<td>0.00408(18)</td>
<td>0.99998</td>
<td></td>
</tr>
<tr>
<td>GB</td>
<td>5.73(25)x10(^{-5})</td>
<td>0.00171(3)</td>
<td>0.9969</td>
<td>15</td>
</tr>
<tr>
<td>GB + Al</td>
<td>5.47(28)x10(^{-5})</td>
<td>0.00182(3)</td>
<td>0.9956</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Phantom</th>
<th>Slope</th>
<th>Intercept</th>
<th>( r^* )</th>
<th>Mean Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(m(^3) Kg(^{-1}))</td>
<td></td>
<td></td>
<td>(Kg m(^{-3}))</td>
</tr>
<tr>
<td>( \text{K}_2\text{HPO}_4 )</td>
<td>0.395(5)</td>
<td>-0.325(5)</td>
<td>0.9988</td>
<td>6.7</td>
</tr>
<tr>
<td>( \text{K}_2\text{HPO}_4 + \text{Al} )</td>
<td>0.407(5)</td>
<td>-0.336(6)</td>
<td>0.9972</td>
<td></td>
</tr>
<tr>
<td>PEPHA</td>
<td>3.21(5)x10(^{-4})</td>
<td>0.0137(6)</td>
<td>0.9997</td>
<td>2.7</td>
</tr>
<tr>
<td>PEPHA + Al</td>
<td>3.25(6)x10(^{-4})</td>
<td>0.0142(6)</td>
<td>0.9996</td>
<td></td>
</tr>
<tr>
<td>GB</td>
<td>2.60(10)x10(^{-4})</td>
<td>0.00664(10)</td>
<td>0.9999</td>
<td>17</td>
</tr>
<tr>
<td>GB + Al</td>
<td>2.73(12)x10(^{-4})</td>
<td>0.00673(12)</td>
<td>0.983</td>
<td></td>
</tr>
</tbody>
</table>

* \( r = \) Linear Correlation Coefficient
Influence of Aluminium on Rcc
K2HPO4 Phantoms

Scattering Ratio Rcc

0.06
0.05
0.04
0.03
0.02
0.01
0
0.9 0.95 1 1.05 1.1 1.15 1.2 1.25 1.3 1.35 1.4

Relative Density

O  No Al  ▲  Al Tube

Fig. 4.56

Influence of Aluminium on Rct
K2HPO4 Phantoms

Scattering Ratio Rct

0.3
0.25
0.2
0.15
0.1
0.05
0
0.9 0.95 1 1.05 1.1 1.15 1.2 1.25 1.3 1.35 1.4

Relative Density

O  No Al  ▲  Al Tube

Fig. 4.57
Influence of Aluminium on Rcc
GB Phantoms

Influence of Aluminium on Rct
GB Phantoms

Fig. 4.60

Fig. 4.61
Effect of Al on Multiple Scatter

- No Phantom
- Al tube only

Fig. 4.62
alone is placed in the system, bearing in mind that the primary scattering volume is completely within this tube and does not touch its walls. In both cases the peak areas are insignificant compared to those found for bone phantoms and so no correction is necessary. It is apparent that the aluminium increases both the coherent and Compton peak areas lending support to the theory of partial cancellation of the multiple scattering, though the Compton peak is noticeably broadened on the high energy side. This is due to multiple scattering events in which the photon has lost less energy than it would have in a single Compton scattering interaction.

4.5 Experiments Using Gadolinium-153

\(^{153}\text{Gd}\) was used as a gamma-ray source for coherent to Compton ratio (\(R_{CC}\)) experiments by Stalp and Mazess (STA 80), and they considered that it gave better results than the more conventional \(^{241}\text{Am}\). No other commercially available radio-nuclide has been used for such experiments though Leichter et al (LEI 84) did use \(^{133}\text{Xe}\) (81 KeV) and \(^{99}\text{Tc}^m\) (140 KeV) when investigating the energy dependence of \(R_{CC}\). Kerr et al (KER 80) did their experiments with \(^{153}\text{Sm}\) (103 KeV) but this has a short half-life (46.8 hrs.) and thus its use on a day to day basis requires the services of a reactor for regular production.

4.5.1 Experimental Apparatus

The higher photon energies of \(^{153}\text{Gd}\) (97 & 103 KeV)
30 Degrees scatter Gd-153 source

Fig. 4.63
compared with $^{241}\text{Am}$ (60 KeV) decreases the magnitude and increases the forward peaking of the differential cross-sections, thus large scattering angles will have prohibitively low count rates. As the specific activity available is higher than for $^{241}\text{Am}$ it is possible to use smaller scattering angles but the choice is limited by the need to be able to separate the elastic and inelastic peaks. For these experiments an angle of 30 degrees was adopted as it gave a suitable dispersion of the scattered photons as can be seen in Fig. 4.63. It was not possible to use the coherently scattered X-rays from the $^{153}\text{Gd}$ as the spectrum in this region was too complex to separate the elastic and inelastic peaks.

The apparatus used was the same shown in Fig 4.2 except, of course, the source used was $^{153}\text{Gd}$ and not $^{241}\text{Am}$, and the collimator for the source holder had a circular cross-section 5 mm in diameter. This arrangement gave a scattering volume of $2.1 \times 10^3 \text{ mm}^3$ and a maximum linear dimension of 42 mm. The collection time was 43200 s (12 hrs.) which was equivalent to a counting time of 1000 s with a new source. Delivered dose was estimated to be 14 mGy, though most of this is due to the Eu K X-rays emitted by the source with only 5 mGy resulting from the gamma-rays of interest.

Peak area estimation for the coherent scattering was done with the fitting routines discussed in section 4.2.4, and in order to maximise the counting statistics for the coherent to Compton ratio the two elastic peak areas were summed together
and divided by the total area of the Compton peaks. The transmission measurements were again made using the HpGe, 1 mm of brass and 0.80 mm thickness of lead being used to restrict the dead time to below 1%. In a practical system it would not be realistic to have a second HpGe, the transmitted counts were therefore summed together to simulate a low resolution detector. The coherent to transmission ratio was found by dividing the total elastic peak area by this figure.

4.5.2 Scattering from Bone Phantoms

Using the $K_2HPO_4$ solutions to represent bone the normalised curves shown in Fig. 4.64 were produced. The advantage of $R_{ct}$ over $R_{cc}$ in terms of sensitivity, i.e. slope of the curves, is again apparent and the statistical precisions achievable were 6.2 and 9.5 Kg m$^{-3}$, respectively.

For the PEPHA and GB phantoms Fig. 4.65&66 display the dependence of the scattering ratios on the BMC. As was found for the $^{241}$Am there is a marked difference between the two sorts of bone phantoms. The precisions possible were 4.0 ($R_{cc}$) and 3.3 ($R_{ct}$) Kg m$^{-3}$ for the PEPHA phantoms and 8.1 ($R_{cc}$) and 5.9 ($R_{ct}$) for the GB ones.

Comparing these results with the figures obtained for $^{241}$Am, Table 4.7, it can be seen that the two sources give comparable sensitivities though the benefit of $R_{ct}$ over $R_{cc}$ is more marked for the $^{153}$Gd scattering. The latter source
Rct & Rcc (Normalised) for 30 Degrees
Gd-153 Source

Fig. 4.64
Table 4.7 Comparison Between Gd-153 and Am-241

dp (Kg m\(^{-3}\))

<table>
<thead>
<tr>
<th>Phantom</th>
<th>Am-241</th>
<th>Gd-153</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(R_{cc})</td>
<td>(R_{ct})</td>
</tr>
<tr>
<td>(K_2HPO_4)</td>
<td>8.2</td>
<td>3.5</td>
</tr>
<tr>
<td>PEPHA</td>
<td>3.5</td>
<td>3.4</td>
</tr>
<tr>
<td>GB</td>
<td>6.1</td>
<td>5.5</td>
</tr>
</tbody>
</table>

N.B. The error for the \(K_2HPO_4\) is in terms of density whereas for the PEPHA & GB phantoms it is in terms of BMC.
Fig. 4.65

Rcc For PEPHA & GB Phantoms
Gd-153

0.06
0.05
0.04
0.03
0.02
0.01
0

0 50 100 150 200 250 300
Bone Mineral Concentration / Kg m-3

○ Pepha ▼ Gb

Fig. 4.66

Rct For PEPHA & GB Phantoms
Gd-153

0.7
0.6
0.5
0.4
0.3
0.2
0.1

0 50 100 150 200 250 300
Bone Mineral Concentration / Kg m-3

○ Pepha ▼ Gb
does however deliver considerably higher dose than that arising from the use of $^{241}\text{Am}$.

4.5.3 Influence of Size and Overlying Material

To examine the effects of sample size on the accuracy of the scattering measurements the results for the $\text{K}_2\text{HPO}_4$ solutions in 40 mm and 50 mm diameter bottles were compared, as before, the results are shown in Figs. 4.67&68. It is clear that the $R_{ct}$ curves are significantly affected by the change in size. When the scattering from the 97 and 103 KeV gamma-rays are considered separately rather than summed together the same deviation is still found. This size dependence will be due to multiple-scatter and it is possible that the use of a smaller scattering angle increases the magnitude of this problem compared with the 70 degrees used with $^{241}\text{Am}$.

For $R_{cc}$ the discrepancy between the curves is less marked but nonetheless the least squares fit to a straight line shows significant differences, the slope of the line is $(6.27 \pm 0.09) \times 10^{-2} \text{ m}^3 \text{ Kg}^{-1}$ for the 50 mm samples compared with $(5.97 \pm 0.08) \times 10^{-2} \text{ m}^3 \text{ Kg}^{-1}$ for the 40 mm diameter ones.

Time restrictions meant that the experiments on the effects of overlying cortical bone, using the aluminium tube to simulate the cortex, could only be done for the PEPHA phantoms. The results obtained are shown in Figs. 4.69&70 and the details of the fitted lines given in Table 4.7. Again the differences
Effect of size on $R_{cc}$
Gd-153

Scattering Ratio $R_{cc}$

0.1
0.08
0.06
0.04
0.02
0

0.9 1 1.1 1.2 1.3 1.4 1.5 1.6 1.7 1.8

Relative Density

○ 50 mm Diameter  ▼ 40 mm Diameter

Fig. 4.67

Effect of size on $R_{ct}$
Gd-153

Scattering Ratio $R_{ct}$

1
0.8
0.6
0.4
0.2
0

0.9 1 1.1 1.2 1.3 1.4 1.5 1.6 1.7 1.8

Relative Density

○ 50 mm Diameter  ▼ 40 mm Diameter

Fig. 4.68
Influence of Aluminium on Rcc
PEPHA Phantoms Gd-153

Fig. 4.69

Influence of Aluminium on Rct
PEPHA Phantoms Gd-153

Fig. 4.70
are significant.

It has to be concluded that a scattering technique, be it $R_{ct}$ or $R_{cc}$, based on $^{153}$Gd as the photon source is susceptible to significant errors in bone mineral estimation induced by changes in sample size and the effects of overlying cortical bone.

4.6 Conclusions

It has been demonstrated that for bone densitometry a scattering technique using the elastically scattered photons corrected for beam attenuation by transmission measurements gives a greater sensitivity than the coherent to Compton ratio often used. The possible errors due to changes in sample size and overlying material were shown to be less than the statistical precision of a single measurement for both scattering techniques using $^{241}$Am as the gamma-ray source. For spongiosa however the advantage in $R_{ct}$ over $R_{cc}$ was not large and it is questionable whether the gain in sensitivity is worth the added cost of a second detector, albeit a low resolution one, and the increased complexity of the measurement procedure which requires two scattering spectra to be collected rather than just the one needed to find $R_{cc}$.

The use of $^{153}$Gd as an alternative gamma-ray source to $^{241}$Am does not appear to be viable. Not only does it have a short half-life, necessitating regular source changes, but to achieve similar sensitivity to an $^{241}$Am system a significantly
higher dose is delivered due to the lower energy photon emissions present in the source spectrum. It was also found to be more susceptible to multiple scattering in the surrounding materials giving rise to significant errors in density or BMC determination.
CHAPTER 5 GAMMA-RAY TRANSMISSION TOMOGRAPHY

5.1 Introduction

The use of computerised tomography using either X- or gamma-rays, as a method of bone densitometry has been discussed in Section 2.6. This chapter covers the experimental work done in building a simple gamma-ray transmission tomography scanner and the results obtained from scanning bone phantom materials, using both single and dual energies.

In photon transmission tomography the aim is to produce a cross-sectional image (2-D map) of the linear attenuation coefficients. A series of transmission scans, as shown in Fig. 5.1, are made at many different orientations. These give measurements of the line integrals of attenuation along the beam paths, as defined by the collimation. These are known as raysums, \( P \), where:

\[
P(\theta, x') = \int u(x', y') \, dy'
\]  

(5.1)

A complete set of raysums for a given angle is known as a projection.

If the unattenuated photon intensity is \( I_0 \) and the measured intensity for a given ray is \( I(\theta, x') \) then:

\[
P(\theta, x') = \ln\left(\frac{I_0}{I(\theta, x')}\right)
\]  

(5.2)
Fig. 5.1 Representation of tomographic scanning. The density function is defined by the $x,y$ co-ordinates and the raysums by $x', \phi$.

(From J Sanders, 1982, Ph D. Thesis, Univ. of Surrey)
From these it is possible to recover, at least approximately, the original distribution $u(x,y)$ using suitable reconstruction algorithms.

The geometry depicted in Fig. 5.1 is that of a first generation scanner (WEB 87): most modern, higher generation, scanners employ a fan-beam geometry with multiple-detector arrays.

5.2 Experimental Apparatus

5.2.1 Mechanics

As the scanner was intended for examining small test objects it was simpler, from a mechanical point of view, to have the source and detector fixed, and move the sample through the collimated gamma-ray beam, than to adopt the usual configuration where the source and detector are on a gantry that moves around the object being scanned. The components used were a commercially available rotary table (Time and Precision Ltd.) mounted on a linear bed manufactured in the mechanical workshops at Surrey University, see Fig. 5.2. Both were controlled by stepper motors and the system backlash was measured at less than 0.1 mm, well below the spatial resolution of the collimators employed.

5.2.2 Gamma-ray Sources and Detector

Financial limitations precluded the use of multi-detector
Fig. 5.2 Photographs of the tomography apparatus.
arrays and thus the fan-beam geometry of commercial equipment. Instead a single sodium iodide detector (NaI(Tl)) had to suffice. This had nominal crystal dimensions of 25 mm depth by 38 mm diameter (1" by 1.5"). Scanning the face of the detector in the same manner as for the HpGe detector (Section 4.2) gave its active area as $1132 \pm 5 \text{ mm}^2$. Fig. 5.3 shows the intrinsic photopeak efficiency of the detector as a function of energy, the value for the 59.5 KeV peak of $^{241}\text{Am}$ being 0.71(4). To reduce the effects of background radiation this detector was mounted in a steel shield into which could be fitted brass re-inforced lead collimators as shown in Fig. 5.4. The collimators were 10 mm long and had cylindrical bores of 1 or 2 mm diameter. With the source and detector separation typically being 112(1) mm count rates of $130 \text{ s}^{-1}$ and $2.3\times10^3 \text{ s}^{-1}$ were obtained for the 1 & 2 mm collimators respectively. Most of the work was done with the larger size to reduce the scanning time.

The majority of experiments were done using a 7.4 GBq (200 mCi) $^{241}\text{Am}$ source with an active diameter of 5 mm. Once again this was steel encapsulated and thus provided a mono-energetic 59.5 KeV photon flux. This ensured freedom from beam-hardening (i.e. differential attenuation of the various energies in the scanning beam). Dual-energy scans were done using the borrowed $^{153}\text{Gd}$ source discussed in Section 4.5. As the scintillation detector has a much lower resolution than the HpGe the measured spectrum, Fig. 5.5, contains just two main peaks corresponding to the Eu K X-rays (41 to 50 KeV) and the 97 and 103 KeV gamma-rays. The 70 KeV line is also discernible but is of too low an

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Nal(Tl) Detector Intrinsic Photopeak Efficiency

Fig. 5.3
Fig. 5.4 Source and detector for tomography scanning

Notes:
1. Nal(Tl) Detector
2. Test Object
3. Source
4. Steel
5. Lead
6. Brass
Gd-153 Spectrum Using NaI(Tl) Detector

Eu K X-rays

97 & 103 KeV

Counts

Channel No. $\times 10^2$

Fig. 5.5
intensity to be of interest. Both of these sources were mounted in a lead and brass holder, again with interchangable collimators of the same dimensions as for the detector, Fig.5.4.

Correct reconstruction of the image requires that the centre of rotation for the projections be known (FOS 81), and for convenience this usually corresponds to the central raysum. To ensure the correct alignment of the apparatus the source holder was designed to allow the radio-isotope to be replaced by a laser the beam of which, shining through both collimators, could be used as a reference line to centre the linear scanning bed.

5.2.3 Electronics and Computer Control

The counting electronics used are shown schematically in Fig. 5.6. High voltage supply, amplifier and dual single channel analysers (SCAs) were contained in a single NIM module. The window for the SCA was set around the photopeak in the gamma-ray spectrum with the aid of an MCA. Output pulses from the SCA had to be stretched to 1 microsecond long to drive the counter-timer and this was done by using a co-incidence unit, that happened to be available, set for a single event only. The counter-timer itself was a low-cost unit that had been constructed in-house by an undergraduate student (HAR 85) and was based on a Motorola MC6840 programmable timer with a maximum count rate capability of 1 MHz and a capacity of 65 532 (i.e. 16 bit binary). Apart from being only one tenth of the cost of a commercial unit it was connected directly to the 1 MHz bus of the BBC micro-computer.
Fig. 5.6 Tomography Apparatus

- BBC Micro-Computer
- Motor Drive Electronics
- Dual Counter Timer
- Pulse Stretcher
- Canberra 1445
- HT Amplifier Dual SCA Novolec 8912
- Source
- Rotary Table
- Linear Drive
- NaI(Tl) Detector
avoiding the need for a separate interface unit. The machine code subroutines to drive the timer were stored as firmware (on an EPROM) in the micro-computer. The author’s contribution to this equipment was in de-bugging this code.

The stepper-motors were controlled from the user port on the micro-computer via commercial driver-cards (RS Components Ltd.). To simplify the control of these motors the necessary bit patterns and clock pulses were generated by machine code subroutines again resident as firmware. The motors themselves moved 1.8 degrees per step and this gave a nominal linear resolution of 0.0125 mm and angular precision of 0.02 for the rotary table.

Overall control of the motors and timer was done using a suite of BASIC programs written by the author but based on similar work in the Physics department at Surrey (McC 86). This software allowed the user to specify the various scanning parameters e.g. number of raysums and projections, linear and angular step size. For the single energy scans the raysums were recorded as the time taken to reach a preset number of counts, usually 1 000, thus ensuring uniform statistical accuracy for all readings and also giving the optimum scan time. In the case of dual-energy scans the second channel on the timer was used, and a second pulse-stretcher, and the raysums recorded as the number of counts received in a preset time. This time being chosen so that the minimum count was about 1 000. All the recorded data were stored on disc for later reconstruction using the algorithms discussed below.
5.2.4 **Image Reconstruction**

The principles of image reconstruction have been reviewed in several places (e.g. BRO 76, KOU 82). In essence, by taking a number of line integrals through a density distribution function it is possible to reconstruct this function. The actual solution of this problem for a finite number of projections has been done both iteratively and analytically.

For this work a widely used analytical method known as filtered back-projection (FBP) was employed. In simple back-projection the magnitude of each raysum is added uniformly to all points in the image that lie along the ray path, thus each point in the reconstructed image is the sum of all the raysums that pass through the equivalent point in the object (BRO 76). This crude approach leads to what is known as star artefacts around dense points as demonstrated in Fig. 5.7&8. In the limit of very large numbers of projections a single dense point will give rise to an image which has a $1/r$ density distribution where $r$ is the distance from the point (KOU 82). By deconvolving this $1/r$ blurring it is possible to recover a true image of the original object. It is possible to do this deconvolution in the Fourier domain but normally it is applied directly to the projection data in real space. As the object is being sampled by a finite number of raysums, $n$, at a linear spacing of $w$ it follows from sampling theory that the maximum spatial frequency in the final image will be given by $k_m$ where:

$$k_m = \frac{1}{2w}$$

(5.3)
Fig. 5.7 Projection data for a circular dense object. (From J Sanders, 1982, Ph D. Thesis, Univ. of Surrey)

Fig. 5.8 Back projection for a circular dense object showing star artefact. (From J Sanders, 1982, Ph D. Thesis, Univ. of Surrey)
and that \( x' \) in eqn. 5.1 can be represented as:

\[
x' = w_i \tag{5.4}
\]

where \( i \) is an integer between 0 and \( n \). Under these conditions it can be shown (BRO 76) that the deconvolved raysums, \( P^* \), can be approximated to:

\[
P^*(\phi, w_i) = \frac{P(\phi, w_i) - \frac{1}{4w} \sum_{i-j, \text{odd}}^{n} \frac{P(\phi, w_j)}{(i-j)^2}}{w} \tag{5.5}
\]

The summation is for all \( j \) such that \( i-j \) is odd.

Back-projecting these corrected raysums introduces a further approximation as they have to be mapped onto a finite grid of pixels, usually \( n \) by \( n \) square, and this involves assigning the values to the picture elements by choosing the nearest neighbour or by linear interpolation. The former requires fewer calculations but the latter, being more accurate was the method adopted here.

For there to be sufficient projections to allow a valid reconstruction it is usually estimated that a minimum of \( \frac{\pi n}{4} \) projections be taken (BRO 76). Most of the images collected on the scanner described here had the same number of projections as raysums.

Two different systems were used for image reconstruction and
analysis. The first one used was an existing facility on the University of Surrey PRIME computers as described by Gilboy et al (GIL 82). Being run on a mini-computer made the reconstructions very rapid (about three or four minutes) but the implementation did not allow sets of images to be reconstructed as batches rather they had to be done one at a time under operator control. The image analysis software drove a SIGMA graphics terminal and allowed the user to extract the average attenuation coefficient of circular regions of interest selected by a cursor as shown in Fig. 5.9. The alternative system was based on the BBC micro-computer, the FBP program being developed from one in general use at Surrey and images being displayed using a PLUTO graphics board and high resolution monitor (BAL 86). Reconstruction times were much longer (about one hour) and memory limitations restricted the image size to 75 x 75 pixels but the fact that data did not have to be transferred to another machine (which included changing the data format) and the ability to set up batch processing to run overnight made this the easier system for the majority of images (which were usually only 45 x 45 or 60 x 60 pixels in size). A further advantage of the micro-computer system was the analysis software which allowed regions of interest to be set by absolute pixel co-ordinates, rather than by subjective manipulations of the cursor, and was therefore able to guarantee a higher degree of reproducibility. When selecting the regions of interest the policy recommended by Banks et al (BAN 86) of choosing the largest area possible was followed.

As discussed above the raysum data were collected as the
Fig. 5.9 Photographs of reconstructed images on the PRIME computer (top) and the BBC micro-computer (bottom).
number of counts, \( N \), collected in a set time or as the time, \( t \), taken to accumulate a set number of counts. The appropriate forms of eqn. 5.2 are therefore:

\[
P(\phi, x') = \ln \left( \frac{N_0}{N} \right)
\]

(5.5)

for preset time where \( N_0 \) is the number of counts recorded for zero attenuation, and:

\[
P(\phi, x') = \ln \left( \frac{t}{t_0} \right)
\]

(5.6)

for preset counts, where \( t_0 \) is the time for zero attenuation. The zero attenuation values were estimated for each projection as the average of the initial and final raysums, care being taken to ensure that the scanned object was smaller than the width of reconstructed area so that these beam paths would be unobstructed. This approach, it was hoped, would reduce the influence of any electronic drifts in the counting chain.

A comparison of the mean linear attenuation coefficients for a set of \( K_2HPO_4 \) solutions as evaluated by the two different reconstruction and analysis systems is given in Fig.5.10. The differences between the two sets of values were within the statistical uncertainties as defined by the standard error of the mean (eqn. 3.4) and were of the order of \( \pm 0.5 \% \) or better. As both reconstruction programs had quite independent histories this agreement can be taken to indicate that both are working correctly. The discrepancy between the experimental values and
Comparing algorithm results with theory
Am-241

Different numbers of projection

Attenuation Coefficient / m-1

Relative Density

Fig. 5.10

Attenuation Coefficient / m-1

Relative Density

Fig. 5.11
those predicted from theory is believed to be due to the influence of scattering and is discussed in section 5.5.

Fig. 5.11 shows the results obtained from scanning $\text{K}_2\text{HPO}_4$ solutions using 45 and 60 projections. The slopes of the fitted lines were $42.4(3)\ m^{-1}$ and $42.3(3)\ m^{-1}$, with intercepts of $-23.6(3)\ m^{-1}$ and $-23.7(3)\ m^{-1}$, for the 45 projection and 60 projection data respectively. This would indicate that the measured attenuation values are not overly sensitive to the acquisition parameters.

5.3 Spatial Resolution

5.3.1 Theory of PSF and MTF

The resolution of an imaging system may be considered in terms of its point spread function (PSF), that is the image resulting from a single impulse, or point object. Following Kouris et al (KOU 82) the object plane can be described as a function $f$ and the image as $g$ where:

$$g(x,y) = L f(x',y') \quad (5.7)$$

$L$ being a linear operator that represents the imaging system. It follows that the PSF can be expressed as a function $h$ where:

$$h(x,x',y,y') = L \delta(x',y') \quad (5.8)$$
In most cases the form of the PSF is the same for all positions within the object plane, i.e. it is spatially invariant, and can be expressed as:

\[ h(x,x',y,y') = h(x-x',y-y') \] (5.9)

By considering an object to be made up of an integral of points it follows that:

\[ g(x,y) = \iint f(x',y') \ h(x-x',y-y') \ dx' \ dy' \] (5.10)
\[ = f(x,y) * h(x,y) \] (5.11)

where \(*\) represents the convolution operator. Taking the Fourier transform of eqn. 5.11 yields:

\[ G(u,v) = F(u,v) H(u,v) \] (5.12)

hence

\[ H(u,v) = G(u,v) / F(u,v) \] (5.13)

where \(G,F \text{ and } H\) represent the Fourier transforms of \(g,f \text{ and } h\); and \(u,v\) are co-ordinates in frequency space. Now \(F\) and \(G\) represent the spatial frequency components that make up the object and image respectively. It follows that \(H\) gives the ratio of these components in the image compared with those in the original object. This function \(H\) is usually referred to as the optical transfer function (OTF) and in an ideal system would be
unity for all frequencies. Generally the modulus of the OTF is the quantity of interest, phase not being important, and is called the modulation transfer function (MTF) and describes the proportion of each spatial frequency that is passed to the image. The coarse features of an object are represented by the low frequencies while the fine detail and sharp edges are the higher frequencies thus the MTF for a system is usually found to fall with frequency indicating the loss of definition in an image. The MTF is multiplicative and so the total MTF for a system will be given by the product of the MTFs for the different stages in the system.

The PSF and MTF are different ways of expressing the same information: the former is a measure of the blurring in real space, the latter describes it in terms of spatial frequencies.

5.3.2 Experimental Determination of the MTF

Using a point object to determine the PSF for a tomography system gives only a small number of points from which to find the function (WHI 81). It is therefore more common (JUD 76) to use an image of a sharp edge to find the edge spread function (ESF), which can be expressed as:

$$\text{ESF}(x) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} h(x,y) \, dy \, dx$$

$$= \text{LSF}(x)$$

where LSF is the line spread function. For an isotropic system
this can be considered to be identical to the PSF (WHI 81).

The resolution of the tomography scanner is limited by the spatial sampling frequency selected and the PSF of the collimators. The former can be readily increased; it is the latter that governs the resolution available. For these experiments the collimators available had apertures 1 and 2 mm in diameter. Smaller bores would have yielded narrower PSFs but at the expense of prohibitively low count rates.

By scanning the collimated photon beam across the edge of an aluminium block, recording the count rate at 0.0125 or 0.025 mm steps (spatial frequencies of 80 and 40 mm\(^{-1}\)) for the 1 and 2 mm diameter collimators respectively, it was possible to find the ESF and, by differentiating, the LSF as shown in Fig.5.12&13. There is a considerable degree of noise present in the LSFs due to statistical variations in the count rates and this is accentuated by the differentiation. This noise is not a problem when the Fourier transform is taken to find the MTF, Fig.5.14, as these high frequency components are beyond the region of interest. The form of these MTFs is what would be expected showing that the higher frequencies are not transferred, the half maxima of the plotted curves corresponding to spatial frequencies of 0.50(2) and 0.90(2) mm\(^{-1}\) for the 2 and 1 mm diameter collimators, respectively.

Tomographs were taken of a simple perspex test object, Fig.5.15, using the two different sized collimators and are shown
Fig. 5.14

Modulation Transfer Function

--- 1 mm Collimation
--- 2 mm Collimation
Hole Diameters
0.5 mm
0.75 mm
1.0 mm
1.5 mm
2.0 mm
3.0 mm
4.0 mm

Fig. 5.15 Perspex Test Phantom.

Fig. 5.16 Image taken with 2 mm collimation.

Fig. 5.17 Image taken with 1 mm collimation.
in Figs. 5.16&17. These images are in rough agreement with the expected limits of resolution of the collimators.

5.4 Background Correction

Due to the presence of other radiation experiments in the laboratory there was found to be a relatively large, and at times quite variable, background count rate. This had to be accounted for in the measurements, especially for the more attenuated raysums where this extraneous radiation increased the apparent transmission by up to 3%. Furthermore this background was found to vary with the sample position as is demonstrated in Fig. 5.18 which shows a projection acquired with the source collimator blocked by a thick (4 mm) lead beam stop. The correction method adopted was to record such a background projection immediately before or after each tomographic image was taken. This was then used to modify the image raysum data. As the test samples were all cylindrical only one background projection was required. Fig. 5.19 shows how the background correction influences the measured attenuation coefficients. Any images that were likely to suffer from variations in the background during the course of the scanning due to the other work in the laboratory were rejected.

5.5 Influence of Photon Scattering

In the simple theory of CT imaging given it was assumed that the photons recorded by the detector were only those that had been transmitted through the material i.e. undergone no
Fig. 5.18
Effect of background subtraction
Am-241

![Graph showing the relationship between Relative Density and Attenuation Coefficient/m⁻¹, with points indicating Uncorrected and Corrected data.](Fig. 5.19)
interactions. In practice scattered radiation is also detected and this leads to artefacts and errors in the measured attenuation values. Techniques to correct for scattering have been published and usually involve subtracting an estimate for the scattered component from the measured signal. This correction factor maybe a fixed fraction of the incident intensity which is assumed to be the same for all the raysums (MOR 83, JOS 82) or maybe estimated from the raysums themselves (HAN 87a).

The fan-beam geometry employed in third and fourth generation scanners (WEB 87a) is likely to be more susceptible to the problems of photon scattering than the single, narrow, collimated gamma-ray beam used for this work. Nonetheless Figs.5.10&23 show clearly the discrepancies, of up to 7%, between the linear attenuation coefficients determined from the tomographs of the K₂HPO₄ solutions (with errors of the order 0.5%) and those expected from calculations based on the tabulations of Hubbell et al (HUB 82) (believed to be accurate to about 2%).

If we consider the usual differential equation describing attenuation of a narrow photon beam of intensity I(x):

\[
\frac{dI(x)}{dx} = - I(x) u(x) dx \tag{5.16}
\]

and include a further term to account for the contribution of forward scattering to beam intensity we obtain:

\[
\frac{dI(x)}{dx} = - I(x) u(x) - \iint u_s(x,y,z,\theta) d\varphi dy dz \tag{5.17}
\]
where $\mu_s$ represents the combined scattering coefficients (for small angles the energy loss due to Compton scattering can be ignored), $\Omega$ is the solid angle subtended by the detector and the integrals over $y$ and $z$ account for the beam divergence and represent the volume of acceptance of the collimators as shown in Fig.5.20. The measured attenuation coefficients will be given by the expression in brackets. It can be seen that the effect of scattering is to reduce the actual attenuation by an amount that depends on the material and also on its position along the length of the raysum path as the width of the acceptance volume and solid angle of the detector vary (MOR 83). If this spatial variation across the reconstructed area in an image is small then the second term in the brackets of eqn. 5.17 will itself be a function of the material only and so it would be possible to characterise materials by their "effective linear attenuation coefficient" as given in eqn. 5.17. This is only valid for narrow beam geometries not fan-beams and does not include contributions from multiple scattering.

For the apparatus used in these experiments no significant variations in the measured attenuation coefficients with size or position were found for the PEPHA bone phantoms or the $K_2HPO_4$ solutions provided the source and detector geometry remained constant. (The experimental errors associated with these measurements were of the order 0.5% to 1%). By altering the geometry quite significant changes in the measured attenuation resulted. Fig.5.21 compares the results obtained from 2 mm diameter detector collimators with lengths of 10 mm and 20 mm.
Fig. 5.20 Geometry for transmission tomography showing the potential scattering volume. (From J Sanders, 1982, Ph D. Thesis, Univ. of Surrey)

Fig. 5.21
The longer collimation will reduce beam divergence and thus the influence of photon scattering is reduced giving larger attenuation values. The slope and intercept for the 10 mm collimators were 44.8(1) m\(^{-1}\) and -26.4(2) m\(^{-1}\) respectively compared with 46.3(2) m\(^{-1}\) and -26.7(2) m\(^{-1}\) for the longer ones. Variations in the attenuation coefficients were also noted when the source and detector separation were altered.

Hangartner (HAN 87a) found that for both X-ray and gamma-ray \(^{125}\text{I}\) tomography scanners (utilising fan beam geometries) surrounding a bone phantom (K\(_2\)HPO\(_4\) solution) with an aluminium cylinder increased the measured attenuation coefficient. This was believed to be due to scattering, the resulting artificially low attenuation value for the aluminium causing the negative terms in the convolved raysums to be reduced.

If the simple theory developed above (eqn. 5.17) is valid then overlying material should not influence the measured attenuation values for narrow beam geometry. This was investigated by scanning the K\(_2\)HPO\(_4\) solutions with an aluminium tube, wall thickness 1.60(5) mm, placed around them (as in section 4.4.4). Fig.5.22 shows the measured attenuations (errors of the order 0.5% or better) for the solutions with and without the aluminium present, the fitted lines having slopes of 42.8(3) m\(^{-1}\) and 42.4(3) m\(^{-1}\) and intercepts of -23.6(3) m\(^{-1}\) and -24.0(3) m\(^{-1}\), respectively. The effect of the aluminium would appear to be insignificant within the limits of the experimental error. For this wall thickness Hangartner's machine yielded differences of
Influence of aluminium
Am-241

Attenuation Coefficient / m⁻¹

Relative Density

Fig. 5.22
between 3% and 7% (HAN 87a).

5.6 Bone Phantoms

Tomographic scans were made of the various bone substitute materials ($K_2HPO_4$ solutions, PEPHA and GB phantoms) to estimate the precision attainable in estimating bone mineral content. To be consistent with the experiments done on gamma-ray scattering the precision is again defined as the uncertainty in the measured density (or BMC), $dp$, as given by:

$$dp = \frac{du}{S}$$  \hspace{1cm} (5.18)

where $du$ is the error (1 s.d.) in the attenuation coefficient and $S$ is the slope of the attenuation coefficient versus density (or BMC) graph.

For all these scans the same source and detector geometry was maintained with 2 mm diameter by 10 mm long collimation for both. All images were recorded as 45 projections, at 4 degree angular increments, and 45 raysums per projection at 2 mm spacing, giving a scan time of two to three hours. Background corrections, as discussed in section 5.4, were applied to each reconstruction. To aid location of the samples a plastic tube with wall thickness of 10 mm and internal diameter of 40 mm, corresponding to the diameter of the phantoms, was stuck on the rotary table. By noting the attenuation coefficient of this tube in each image it was possible to check the scanner’s consistency.
and to guard against any anomalous results. In practice no variations, beyond the expected statistical range, were found.

The results for two separate batches of $\text{K}_2\text{HPO}_4$ solution are shown in Fig.5.23 along with the theoretical values expected demonstrating the effect of scattering. Fig.5.24 shows the attenuation versus BMC curves for the GB and PEPHA phantoms. It can be seen that there are significant differences between the two types of bone substitute due to the different radiation properties of the MSG and petrolatum being used to represent the soft tissues. Table 5.1 gives the parameters of the straight lines fitted to data and the estimated limits of precision. Note that these precisions are quoted in terms of physical density for

<table>
<thead>
<tr>
<th>Phantom</th>
<th>Slope ($m^2 Kg^{-1}$)</th>
<th>Intercept ($m^{-1}$)</th>
<th>$r$</th>
<th>dp ($Kg m^{-3}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL21-31 ($K_2\text{HPO}_4$)</td>
<td>0.0424(3)</td>
<td>-23.6(3)</td>
<td>0.9997</td>
<td>2.7</td>
</tr>
<tr>
<td>BL1-11 ($K_2\text{HPO}_4$)</td>
<td>0.0423(2)</td>
<td>-23.4(3)</td>
<td>0.9998</td>
<td>2.7</td>
</tr>
<tr>
<td>PEPHA</td>
<td>$3.77(6)\times10^{-4}$</td>
<td>15.80(9)</td>
<td>0.9999</td>
<td>3.7</td>
</tr>
<tr>
<td>GB</td>
<td>$3.27(5)\times10^{-4}$</td>
<td>19.62(6)</td>
<td>0.9995</td>
<td>3.1</td>
</tr>
</tbody>
</table>

Precision (dp) has an uncertainty of about 10%.

N.B. The precision is measured in terms of density for the $\text{K}_2\text{HPO}_4$ solutions and as BMC for the PEPHA & GB phantoms.
Different batches of solution
Am-241

Attenuation Coefficient / m-1

Relative Density

0.9 0.95 1 1.05 1.1 1.15 1.2 1.25 1.3 1.35 1.4 1.45 1.5

○ BL 1-11  —— Theory  ▼ BL 21-31

Fig. 5.23

PEPHA and GB Phantoms compared
Am-241

Attenuation Coefficient / m-1

Bone Mineral Concentration / Kg m-3

0 50 100 150 200 250 300

○ PEPHA Phantoms  ▼ GB Phantoms

Fig. 5.24
the solutions and in terms of BMC for the gel phantoms. The estimated dose delivered for a single scan was about 0.1 mGy in agreement with the figures quoted for $^{125}$I isotopic CT scanners (HOS 86).

5.7 Dual Energy Tomography

The availability, for a short while, of a $^{153}$Gd source allowed dual energy tomography scans to be made. As discussed in section 5.2.2 the low resolution of the NaI(Tl) detector does not separate all the spectral lines but it is possible to set two energy windows: one to cover the Eu K X-rays and the other for the 97 and 103 KeV gamma-rays, with nominal average energies of 45 and 100 KeV respectively. The spread in photon energies within these set ranges may suffer from some beam hardening but no obvious signs of this (e.g. "cupping" (BRO 76) or non-linearities in the attenuation coefficients (MOR 83)) were noticed.

All images were collected using the same parameters as for the $^{241}$Am experiments, the collection time being set to ensure that the minimum number of counts in a raysum was 1 000. The dose delivered was estimated to be about 0.2 mGy and scan times were 3 to 4 hours.

5.7.1 Dual Energy Calibration

The theory of dual energy tomography calibration using two reference materials was briefly discussed in section 2.6.2.
Considering equation 2.8:

\[ u(E) = p_w \left( \frac{m_w u_w(E)}{p_w} + \frac{m_r u_r(E)}{p_r} \right) \]  

(2.8)

it is apparent that if the attenuation of the material under test can be found for two different energies then knowing the mass attenuation coefficients for water and the chosen reference material at these energies will allow the parameter \( m_r \cdot p_w \) to be found. This represents the mass of the reference material per unit volume, in aqueous solution, equivalent to the measured attenuation coefficients.

The obvious candidate for a reference material was \( \text{K}_2\text{HPO}_4 \), especially as aqueous solutions of known concentrations were already to hand. Fig.5.25 shows the measured attenuation coefficients for the two energies. The mass attenuation coefficients were found by linear least-squares fitting of equation 2.8 to these results and the values are given as a footnote in Table 5.2.

5.7.2 Bone Phantoms

Dual energy scans of the TBL phantoms (\( \text{K}_2\text{HPO}_4 \) plus a liquid red marrow substitute) yielded results in excellent agreement with the true concentrations of the phosphate as is shown in Table 5.2. The results of tomography scans at 60 KeV for the TBL phantoms and the pure \( \text{K}_2\text{HPO}_4 \) solutions (BL phantoms) are shown in Fig. 5.26 where discrepancies are apparent. Fig.2.27 plots the
K2HPO4 phantoms
Gd-153

Attenuation Coefficient / m⁻¹

Relative Density

Fig. 5.25

○ 45 KeV  ▼ 100 KeV
results of Table 5.1 and the fitted line has a slope of 1.00(2) and an intercept at -3(5) Kg m\(^{-3}\) indicating, within the errors, perfect correlation between the estimated and actual values. The use of K\(_2\)HPO\(_4\) as both the reference material and the cortical bone substitute in this case is an ideal situation and hence the reason for this good agreement. But it also indicates the power of this technique when sensible reference materials are used (BUR 87).

Scans were also made of the PEPHA and GB phantoms and the results for the two different energy ranges are given in Figs.5.28&29. Using these to find the equivalent concentrations of K\(_2\)HPO\(_4\) gives the graph shown in Fig.5.30. It will be noted

<table>
<thead>
<tr>
<th>Phantom</th>
<th>Mass of K(_2)HPO(_4) / unit volume (Kg m(^{-3}))</th>
<th>(m_r p_w) (Kg m(^{-3}))</th>
<th>Error (Kg m(^{-3}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBL1</td>
<td>0</td>
<td>-5</td>
<td>9</td>
</tr>
<tr>
<td>TBL2</td>
<td>67.8</td>
<td>60</td>
<td>9</td>
</tr>
<tr>
<td>TBL3</td>
<td>135.5</td>
<td>131</td>
<td>9</td>
</tr>
<tr>
<td>TBL4</td>
<td>233.3</td>
<td>235</td>
<td>8</td>
</tr>
<tr>
<td>TBL5</td>
<td>327.8</td>
<td>330</td>
<td>8</td>
</tr>
<tr>
<td>TBL6</td>
<td>426.3</td>
<td>431</td>
<td>8</td>
</tr>
<tr>
<td>TBL7</td>
<td>641.8</td>
<td>634</td>
<td>8</td>
</tr>
</tbody>
</table>

The above estimates were based on the following empirically determined mass attenuation coefficients:

<table>
<thead>
<tr>
<th>Energy (KeV)</th>
<th>((u/p)_w) (m(^2) Kg(^{-1}))</th>
<th>((u/p)_r) (m(^2) Kg(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>0.0234(3)</td>
<td>0.0729(1)</td>
</tr>
<tr>
<td>100</td>
<td>0.0161(2)</td>
<td>0.0183(1)</td>
</tr>
</tbody>
</table>
PEPHA and GB Phantoms compared
Gd-153 (45 Kev)
PEPHA and GB Phantoms compared
Gd-153 (Dual Energy)

Mr. Pw (K2HPO4) / Kg m-3

Bone Mineral Concentration / Kg m-3

○ PEPHA Phantoms   ▽ GB Phantoms

Fig. 5.30
Table 4.3 Differences Between Bone Phantoms

<table>
<thead>
<tr>
<th>Energy (KeV)</th>
<th>Difference (Kg m$^{-3}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>64(2)</td>
</tr>
<tr>
<td>60</td>
<td>75(5)</td>
</tr>
<tr>
<td>100</td>
<td>110(5)</td>
</tr>
<tr>
<td>45 + 100</td>
<td>40(11)</td>
</tr>
<tr>
<td>(Dual energy)</td>
<td></td>
</tr>
</tbody>
</table>

The difference is defined as:

\[
\frac{u_{GB}(200) - u_{PEPHA}(200)}{S}
\]

where $S$ is the slope of the attenuation versus BMC curve for the PEPHA phantoms and the attenuation coefficients are evaluated for BMC = 200 Kg m$^{-3}$.

that there is still a discrepancy between the two bone phantom sets. Table 5.3 shows this difference for the various energies expressed in terms of the error in estimated BMC between the two types of phantom for BMC of 200 Kg m$^{-3}$. It is apparent that for single energy scans the lower the energy the smaller the difference. This is due to the greater influence of the bone mineral, when compared with the soft tissue substitute, on the total attenuation as the photon energy decreases, as discussed in section 2.6.3. The dual energy measurements, however, provide the smallest difference of all i.e. the estimates of BMC are influenced by the differences in the soft tissue substitutes to a smaller extent than the other methods. This is in agreement with published work on dual energy X-ray tomography which has demonstrated that this technique is less susceptible to the
This greater accuracy is, however, at the expense of overall precision as two separate measurements have to be combined. Table 5.4 summarises the precisions in BMC evaluation attainable for single and dual energy tomography with the $^{153}$Gd source.

<table>
<thead>
<tr>
<th>Phantoms</th>
<th>45 KeV</th>
<th>100 KeV</th>
<th>45 + 100 KeV (Dual energy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$K_2HPO_4$</td>
<td>1.4</td>
<td>4.0</td>
<td>-</td>
</tr>
<tr>
<td>PEPHA</td>
<td>2.1</td>
<td>5.9</td>
<td>7.7</td>
</tr>
<tr>
<td>GB</td>
<td>1.5</td>
<td>5.1</td>
<td>7.6</td>
</tr>
</tbody>
</table>

Uncertainties in estimates of precision are roughly 10%.

5.8 Conclusions

The simple gamma-ray tomography scanner built for these experiments has demonstrated its ability to assess the bone mineral content of bone phantoms with a high degree of precision (of order 1%). In terms of accuracy however there were problems due to photon scattering giving rise to artificially low attenuation values. By ensuring the source and detector geometry remained unaltered it was possible to use the "effective
attenuation coefficients", i.e. those found empirically, to make comparative measurements. These appeared to be consistent and they were dependent only on the given material and were not affected by other parts of object e.g. the presence of the aluminium tube. But these values are a function of a given source and detector collimation and may vary with position in the object. At best they will be specific to a given instrument and comparisons between different machines could only be made with reference to calibration materials and not by absolute measurements of the attenuation coefficients.

It was possible to use the measured attenuation coefficients to characterise materials because these were independent of any other materials in the objects being scanned, this in turn being due to the simple, single beam geometry. For the majority of tomography scanners in current use this will not be the case as their fan beam geometries allow the recorded raysums to be influenced by scattering from other regions in the object giving rise to interference in the measured attenuation coefficients from surrounding materials (HAN 87a).

Dual energy tomography using a gamma-ray source rather than X-rays has been demonstrated to yield good results for the simple bone substitutes used here. This, along with the results from similar experiments by More et al (MOR 87), suggests that a dual energy gamma-ray tomography scanner specifically for examining peripheral sites may yield useful results. Obtaining a suitable source (or sources) with sufficient intensity to keep
scan times acceptably short may, however, prove difficult, and again the problems of scattering will have to be addressed.
6.1 Bone Tissue Substitutes

The simple bone tissue substitutes used in this work seemed to perform adequately but as stressed in Section 4.6 none of them could be considered to be ideal. In terms of ease of preparation and of assessing their composition solutions of $K_2HPO_4$ do seem to be the most suitable if demands for exact elemental equivalence can be relaxed.

The importance of good calibration phantoms for X-ray transmission tomography measurements on bone tissue has prompted recent work into the use of hydroxyapatite distributed in water equivalent plastics (KAL 87, LON 87). With dual energy tomography also needing suitable reference materials for calibration this would appear to be an area of active interest. Attention should be drawn to the need for phantom materials to model not only photon linear attenuation but also the scattering cross-sections. This is not only of importance to direct measurements of photon scattering but also to transmission CT where scattered radiation has a significant influence on the measured values of the attenuation coefficients.

6.2 Gamma-ray Scattering

It was demonstrated that the technique proposed by Kerr et al (KER 80) for bone densitometry using coherent gamma-ray
scattering, normalised by separate transmission measurements ($R_{ct}$), did offer improved sensitivity over the coherent to Compton scattering ratio ($R_{cc}$) originally proposed by Puumalainen et al (PUU 76). The improvement offered, however, was not very great (of order 10% or less) especially for the range of scattering cross-section values expected from trabecular bone. An attractive feature of the ratio method, $R_{cc}$, is that only one scattered spectrum need be recorded whereas the transmission corrections require two such spectra plus associated transmission measurements, ideally done on a second detector. It is likely that the simplicity of the coherent to Compton ratio would offset the small loss in sensitivity to make it the preferred one of the two.

Of the two sources tried $^{241}$Am gave the lower dose, 4 mGy as opposed to the 14 mGy for the $^{153}$Gd, and was less susceptible to the problems of multiple-scattering. Possible avenues for future research would be to investigate ways of filtering the unwanted components from the $^{153}$Gd to reduce the dose (though this will require a much brighter source to cope with the attenuation of the useful gamma-ray lines) and to examine the possibilities of other photon sources. Another field of study could be the problems associated with multiple-scattering and the limits this imposes on accuracy, sample size etc. The best way to approach this may be to use some form of Monte-Carlo modelling program.
6.3 Gamma-ray Transmission Tomography

The linear attenuation coefficients, as measured by tomographic imaging, were found to be artificially low due to the influence of photon scattering. For the first generation scanner used in this work it was possible to rely on the "effective linear attenuation coefficients" and these gave consistent results independent of the sample size or any overlying materials. This approach would probably not be valid on a fan beam geometry scanner as the single scattering is not confined to a narrow beam and thus interference between different regions in the object can occur (HAN 87a). Further work in this area must be considered essential if reliable estimates of bone mineral content are to be made using tomography scanners.

Dual energy tomography using the $^{153}$Gd was shown to give greater accuracy, albeit with reduced precision, in determining bone mineral content as it was less susceptible to soft tissue variations. This is in accord with the results obtained for dual energy X-ray CT (e.g. ADA 82, BUR 87). The advantages of an isotope-based dual energy tomography system for scanning distal sites in terms of cost and dose delivered may make it an interesting avenue for future work (MOR 87) especially if sufficiently bright sources can be found to keep scan times acceptably low. The experimental system described in Chapter 5 used 7.4 GBq (200 mCi) of $^{241}$Am and took at least two hours to collect an image and was therefore only suitable for simple studies on small samples.
6.4 Comparing the Two Techniques

Table 6.1 summarises the precisions available for BMC determination with the scattering and tomographic techniques studied. It must be stressed that these are the results of experiments done under ideal conditions on homogeneous samples. The precisions of these methods when applied in a clinical context would probably be two or three times worse (HAN87b).

<table>
<thead>
<tr>
<th>Method</th>
<th>dp (Kg m(^{-3}))</th>
<th>Dose (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(K_2HPO_4)</td>
<td>PEPHA</td>
</tr>
<tr>
<td>(^{241})Am</td>
<td>Rcc</td>
<td>8.2</td>
</tr>
<tr>
<td></td>
<td>Rct</td>
<td>3.5</td>
</tr>
<tr>
<td>(^{153})Gd</td>
<td>Rcc</td>
<td>9.5</td>
</tr>
<tr>
<td></td>
<td>Rct</td>
<td>6.2</td>
</tr>
<tr>
<td>CT (60KeV)</td>
<td></td>
<td>2.7</td>
</tr>
<tr>
<td>CT (45KeV)</td>
<td></td>
<td>1.4</td>
</tr>
<tr>
<td>CT (Dual Energy)</td>
<td></td>
<td>-</td>
</tr>
</tbody>
</table>
It is clear that while scattering measurements can offer comparable precision to tomographic imaging this is at the expense of a much higher dose. The latter has the added advantage of producing a picture of the examination site which may provide additional information of use in medical diagnosis and also guarantees that the trabecular and cortical bone can be distinguished. For gamma-ray scattering it is foreseeable that regions of compact bone may be included in the volume interrogated thus making the average BMC of what was thought to be spongiosa higher than it ought to be.

Both techniques suffer from inaccuracies due to soft tissue variability though dual energy tomography does appear to offer a solution to that problem. A further problem common to both techniques is unwanted photon scattering. The influence of this on transmission tomography depends very much on the scanner geometry and for the simple experimental scanner it was not a severe problem as the attenuation coefficients were not affected by sample size or overlying materials. It is known however that coherent to Compton ratios can be significantly influenced by soft tissue surrounding the skeletal site examined (LIN 82) and it is therefore restricted to regions where the bone is immediately subcutaneous. This, coupled with the need for a reasonable volume of cancellous bone, probably limits its use to studies of the calcaneus (heel bone) alone. The overwhelming advantage of the scattering ratio method is its simplicity, requiring only a suitable source (e.g. 40 GBq of $^{241}\text{Am}$) and a high resolution detector, with associated electronics, and the
only mechanical requirements being collimation to define the interaction volume and a suitable jig to help position and support the examination site e.g. the heel.

Some clinical work has been done using coherent to Compton scattering (SHU 86&87) and it maybe that the technique may demonstrate some advantage over other, rival, methods. The author's opinion, however, is that while photon scattering may have applications in the field of non-destructive testing (HOL 84) it is not the most suitable method for determining bone mineral concentration in-vivo. On the other hand gamma-ray transmission tomography would appear to offer a powerful means of examining bone tissue at peripheral sites for only a low radiation dose.
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