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Radiation dosimetry considerations for skeletal survey imaging of multiple myeloma

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ABSTRACT

Purpose: This paper aims to review the dosimetry and utility of currently implemented imaging modalities for assessment of multiple myeloma and consider the role of tin filtration computed tomography (CT) as a potential replacement to current standard practice.

Methods: Radiation output of tin CT was measured experimentally and used for software-based dose calculation. Resultant effective dose was then compared to calculated planar radiography doses and published doses of other imaging modalities.

Results: Based on example patient parameters used for modalities and 14 projection planar radiography site protocols, doses are comparable between planar radiography and tin filtration CT (approximately 0.9 and 1.0 mSv respectively). Both studies carried a reduced radiation burden compared to Expected Pathologically Increased Contrast-CT (EPIC-CT), FDG-PET and MIBI SPECT/CT (5.7, 11.1–20.0 and 13.0 mSv respectively).

Conclusion: Tin filtered CT provided visualisation of multiple myeloma at doses comparable to planar radiography and where available may be a suitable alternative, following due consideration of patient specific justification and optimisation in line with best practice.

1. Introduction

Multiple myeloma is a haematological disease in which clonal expansion of neoplastic plasma cells in the bone marrow causes production of monoclonal immunoglobulin [1,2]. The neoplastic plasma cells interact with the bone and bone marrow microenvironment commonly resulting in both local and generalised bone resorption leading to osteopenia and the formation of osteolytic ('lytic') lesions, visible under radiological and nuclear medicine examination as focal regions of low bone density. The presence of myeloma related bone disease is the most frequent cause of the debilitating symptoms, pain and pathological fractures, in addition to anaemia, hypercalcaemia and renal failure [3,4]. The detection of lytic bone disease is important even in patients without bone related symptoms at diagnosis, as urgent local treatment may prevent pathological fracture and also change the diagnostic grading from smoldering multiple myeloma (SMM) requiring monitoring but not immediate treatment, to multiple myeloma requiring systemic therapy [5]. The global incidence of myeloma was 2.1 per 100,000 in 2016 with an age-standardised death rate of 1.5 per 100,000 and 5-year life expectancy of 1 in 2 [6,7].

The imaging component of multiple myeloma diagnosis can be performed with a number of modalities: Computed Tomography (CT), 99mTc-Sestamibi Single Photon Emission Computed Tomography (MIBI SPECT/CT), 18F-Fluoro-DeoxyGlucose Positron Emission Tomography (FDG-PET/CT), Planar Radiographic Skeletal Survey and a range of Magnetic Resonance Imaging (MRI) sequences, with each method having specific advantages and disadvantages that must be understood to ensure appropriate use. Determination of the most appropriate imaging modality must be made on a patient-specific basis and include consideration of disease progression, examination cost, government subsidy status, availability of imaging equipment, radiation burden, imaging time and patient comfort [2,8].

This paper discusses the dosimetry and utility of the above listed imaging modalities for assessment of multiple myeloma. The potential role of tin filtration CT for imaging of multiple myeloma is considered through experimental measurements, exploring potential suitability as an alternative to planar radiography, the current local standard practice.

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2. Materials and methods

2.1. Planar radiography dosimetry

Dosimetric assessment of the radiographic skeletal survey used projections included in the site protocol, with acquisition parameters obtained from a typical patient. This information was then used to simulate examinations in commercial planar radiography Monte Carlo simulation software, PCXMC [9]. Although in the imaging department there are a number of X-ray units from different manufacturers, for the purpose of this study, data from a Siemens Multix™ Fusion (Siemens Healthineers) was used.

2.2. Tin filtration CT dosimetry

Theoretical plausibility of dosimetric benefit from utilization of tin filtration CT was initially evaluated using the commercial spectrum simulation software SpekCalc [10], using scanner specifications from supplied system owner's manual.

Experimental measurements were obtained from a dual-source CT apparatus (SOMATOM Force; Siemens Healthineers), with an acquisition protocol using 150 kVp, 0.3 mm Ti and 0.5 mm Al of inherent filtration and 0.6 mm of additional Sn filtration. Measurements of Kinetic Energy Released per unit Mass in air (air KERMA), were made with this scanner, using a 100 mm pencil ionisation chamber and associated radiation dosimetry system (X2; RaySafe), in air and in standard 16 cm and 32 cm PMMA phantoms (TO CTDI; Leeds Test Objects). These measurements were used to calculate CT Dose Index (CTDI) and verify the linearity of this scanner's output using multiple mAs values to determine $CTDI_{air}$ across a relevant range.

From these measurements, normalised output CTDI values (${}_{n}CTDI_{w}$) were calculated for head and body phantoms in mGy/100 mAs and compared to data from the manufacturer documentation [11]. These experimentally validated manufacturer ${}_{n}CTDI_{w}$ values were used with manufacturer relative collimation weighting factors to add this as a new scanner to existing CT dosimetry program, ImPACT [12]. This data was then used by ImPACT for scanner performance matching to a predefined library of Monte Carlo datasets, from which organ and effective doses are calculated using entered acquisition parameters.

2.3. Dosimetric assessment of other modalities

A radiation dosimetry evaluation is not necessary for MRI and as such is not included. Assessment of radiation doses delivered by FDG-PET/CT and MIBI SPECT/CT examinations were performed using published effective doses, reference activity values and effective dose coefficients [13–18].

3. Results

3.1. Planar radiography

Table 1 below shows the projections and acquisition parameters obtained from the DICOM header of an example patient undergoing radiographic skeletal survey for multiple myeloma. The final column of this table also lists effective doses, in μSv, determined by Monte Carlo simulation.

3.2. Simulated spectrum characteristics

Output beam profiles from Aluminium and Tin filters for 150 kVp are compared in Table 2 and show a substantial increase in 1st HVL for tin compared to no tin. Additionally, output per unit mAs from Bremsstrahlung and Characteristic X-rays at 1 m was much lower for tin filtration geometry, compared to conventional aluminium filtration, as shown in Fig. 1.

3.3. Tin filtration CT examination

For addition of the scanner to ImPACT, collimation weighting factors, relative to a reference collimation, are applied to central and peripheral phantom air KERMA measurements to calculate relevant dose values. A comparison of manufacturer and experimentally measured KERMA values are show in Table 3 for each of these required quantities.

3.4. Comparison of effective doses for imaging of multiple myeloma

After measurement of scanner output and confirmation of applicability of published data to specific site scanner, a dose calculation could be performed using ImPACT. The site protocol for tin filtration CT skeletal survey was initially based on that used at other locations, and is summarised in Table 4.

The dose calculated by ImPACT after relevant manufacturer parameters and specific protocol acquisition parameters were added, was 1.0 mSv for tin filtration CT, 0.06 mSv higher than the planar radiographic study. This value was determined using scanner reported average tube current and without consideration of tube-current modulation, an advanced dose adaptation technique not supported by ImPACT. Table 5 provides a summary of these results, along with dosimetry results for the other modalities discussed above.

4. Discussion

In line with the International Commission on Radiological Protection report 103, all medical procedures using ionising radiation must be optimised to deliver only radiation sufficient to achieve desired outcome, societal and economic factors accounted for [19].

Optimisation of a procedure starts with selection of the most appropriate modality, giving due consideration to any associated risks and benefits. Improving clinicians understanding of available imaging modalities will help to ensure the correct decision is reached for each patient.

4.1. Planar radiography

As the most ubiquitous radiation imaging modality, skeletal survey of all bones by planar radiography (also called "projectional radiography" or "general/plain radiography") is a common method for assessment of suspected multiple myeloma. Despite excellent sensitivity in cortical bone lesions, low sensitivity in other areas leads to a quoted false negative rate for planar investigation of multiple myeloma of up to 70% [8,20]. Additionally, the density loss required for visibility on planar radiography is up to 50%, meaning disease progression may be advanced before pathology is visualised [20].

In Australia, radiographic units outnumber CT 3:1 [21], with the distribution of CT scanners in regional and remote areas disproportionately limited. As radiographic examinations carry a reduced radiation exposure for multiple myeloma investigation compared to other imaging modalities many locations, including the site of this investigation, utilise a radiographic skeletal survey as the imaging method of choice [2,5].

4.2. Computed tomography

From 1994 to 2009, the number of CT examinations per capita in Australia has increased by an average of 7.1% each year [21]. Similar levels of growth have been reported across the globe, collectively illustrating the ever-growing utility of CT as a diagnostic tool. Current generation CT scanners routinely use features such as sub-second gantry rotations, model-based iterative reconstruction and dual-energy acquisitions, with direct application of these features to multiple myeloma patient management shown to be beneficial [22–24].

Table 1
Projections for radiographic multiple myeloma protocol skeletal survey.

Body region	Direction	Peak tube Potential (kVp)	Tube-time current product (mAs)	DAP (mGy*cm^2)	Field size dimensions (cm)		Effective dose (µSv)
Cervical Spine	Lateral	73	32.4	330	19.9	28.5	0.03
Chest	Posteroanterior	125	3.3	150	37.5	40.9	0.03
Distal Femur	Anteroposterior	64	6.4	270	34.8	42.4	0.01
Humerus	Anteroposterior	65	4.6	120	41.0	42.5	0.02
Lumbar Spine	Anteroposterior	81	25.6	1080	20.0	42.5	0.26
Lumbar Spine	Lateral	90	36.2	1870	21.1	42.1	0.15
Pelvis	Anteroposterior	73	15.0	850	42.4	34.8	0.12
Proximal Femur	Anteroposterior	75	12.6	750	42.4	34.8	0.17
Skull	Lateral	66	17.2	360	28.1	22.7	0.01
Thoracic Spine	Anteroposterior	77	15.3	460	18.1	42.5	0.09
Thoracic Spine	Lateral	81	13.1	530	21.7	42.5	0.05
						Total	0.94

Table 2
Comparison of output beam profile from Aluminium and Tin filtered spectrums for 150 kVp.

Filtration material	Half value layer (mm Al)		Mean energy (keV)	Output (µGy/mAs at 1 m)	
	First	Second		Bremsstrahlung	Characteristic output
Aluminium	8.38	10.4	68.8	83.0	11.8
Tin	14.5	14.9	98.0	17.1	0.8

Table 3
Manufacturer and end user measured normalised $_n$CTDI$_w$ values.

CTDI phantom diameter (cm)	Manufacturer normalised $_n$CTDI$_w$ (mGy/100 mAs)		Measured mean normalised $_n$CTDI$_w$ (mGy/100 mAs)	
	100 kVp	150 kVp	100 kVp	150 kVp
0–Free air	1.02	6.83	1.07	6.65
16	0.83	5.40	Not measured	5.42
32	0.42	2.92	0.34	2.76

The consideration of radiation doses in CT is a topical issue and one facet of any optimisation process [8,25]. Radiation doses for full body "conventional" CT scans, maintaining the high image quality levels typically seen in radiology, would be in excess of 10 mSv [26]. Although CT scans such as these would differentiate multiple myeloma, where present, from surrounding bone, when looking for pathology that can be visualised with lower radiation doses, such high dose examinations are inconsistent with radiation optimisation practices and are not performed. During investigation of pathology such as multiple myeloma using CT imaging, it is common to use "Low Dose" acquisitions. Low dose CTs require reduced effective dose to the patient, at the expense of less image contrast, so are appropriate for imaging high contrast pathology. Given medical imaging examinations should always be optimised, where only the minimum radiation dose to form a clinically useful image is employed, these scans are only "low" in comparison to higher dose examinations, making this an obvious and unnecessary distinction.

To avoid creating confusion by referring to aluminium and tin CT protocols interchangeably as 'Low Dose', the authors propose aluminium filtered CT examinations that achieve intended diagnostic outcome at reduced radiation dose, be instead referred to as 'expected pathologically increased contrast' CT, or 'EPIC-CT'. A 'standard' EPIC-CT protocol for imaging of multiple myeloma patients could not be found in the literature, however, the reported doses for EPIC-CT were 1.3–3 times the dose of planar radiography, due to variation in both planar radiography and CT acquisition parameters [5,25].

'Spectral manipulation' as applied to CT is a collective term given to the manipulation of the energies used for image reconstruction. This can refer to dual X-ray tube scanners or multilayer detectors used for

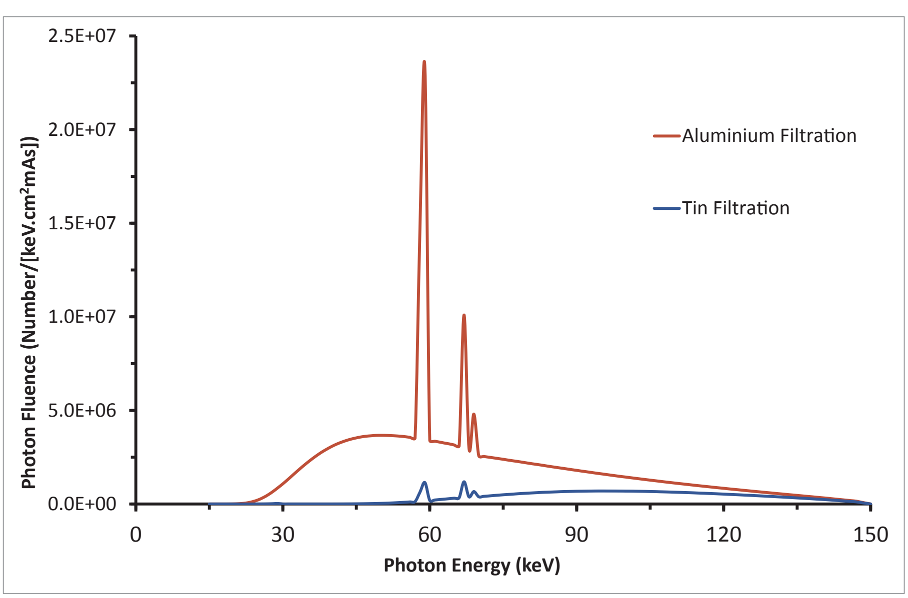

Fig. 1. X-ray spectrum produced following filtration with 6.2 mm of Aluminium, with and without additional 0.6 mm of Tin.

Table 4
Local tin filtration protocol for multiple myeloma.

Reference mAs	Peak tube potential (kVp)	$CTDI_{vol}$ (mGy)	Scan length (cm)	DLP (mGy*cm)
20	150	0.65	104 (Apex to mid-femur)	67
Total collimation width (mm)	No of detectors	Detector width (mm)	Reconstructed slice thickness (mm)	Tube Current Modulation
57.6	96	0.6	1	CareDose

Table 5
Summary of effective doses for imaging of multiple myeloma.

Modality	Effective dose (mSv)
MRI	0.0
Planar Radiography	0.9
EPIC-CT	5.7 [25]
Tin filtration CT	1.0
FDG-PET/CT	11.1–20 [15,18]
^{99m}Tc MIBI SPECT/CT	13.0 [38]

separate reconstructions of 'high' and 'low' energy photon images [27,28]. The dosimetric and clinical benefits of spectral manipulation depend on the particular method and application, and not all intend to reduce radiation dose. In the context of multiple myeloma, spectral manipulation can be used for image reconstruction at specific energies which provide maximum image contrast for lytic lesions, improving visibility.

Both inherent filtration, the absorption of photons by X-ray apparatus components, and added filtration, where known thickness materials are added to further increase beam penetration [29], reduce total X-ray output and image contrast. The amount and type of filtration added is balanced to minimise skin dose and maximise image contrast. Due to the image formation mechanism in CT, the reconstruction process emphasises signal and minimises noise, recovering some contrast and allowing increasingly filtered (or "hardened") X-ray beams to still produce clinical images. The application of aluminium thicknesses four or more times that used in planar radiography is not uncommon. Additionally, some scanners utilise unorthodox filtration materials for shaping of the energy spectrum. The selection of tin for this purpose utilises the increased attenuation coefficient of tin [30] for hardening the beam and has been shown to provide better visualisation of differences in HU values, compared to dual energy acquisitions [20].

4.3. Other modalities: SPECT, PET/CT and MRI

MRI and FDG-PET/CT examinations both provide very different information, however practically suffer similar obstacles. For application in Multiple Myeloma, both modalities have limited or absent government funding and a low number of machines currently installed across Australia, for example, at the time of writing, only 74 sites provided access to PET scanners across the entire country [31,32].

MRI imaging, as the only imaging modality listed utilising non-ionising electromagnetic radiation, has the capacity to image patients without the potentially adverse risk of ionising radiation exposure. The ability of MRI to obtain physiological information through Diffusion Weighted Imaging (DWI) or Dynamic Contrast Enhanced (DCE) better informs diagnosis/staging of focal regions and can allow diagnosis of disease progression before bone demineralisation [33]. The development of increasing magnetic field strengths has greatly reduced the lengthy scanning times commonly seen for MRI examinations. A downside of MRI for multiple myeloma can be poor specificity, as the infiltration of myeloma into bone marrow is imaged, which may not necessarily be associated with the development of lytic lesions and loss of bone density. A further limitation, common to all MRI investigations is suitability/safety criteria which can preclude some patients from being scanned at all. Typical sensitivity for multiple myeloma throughout the body is high for MRI, depending on the acquisition sequences employed, with the exception of cortical bone regions [5,8,34].

In addition to the physiological imaging discussed above, many anatomical acquisition sequences can be performed on MRI, with each emphasising different tissue. T1 and T2 weighted Spin Echo (or Turbo Spin Echo) examinations provide purely anatomical information, with each sequence resulting in better visualisation of bone marrow and fat respectively, due to the difference in relaxation times between tissues. In conjunction with these routine scans, more sophisticated sequences like Short Tau Inversion Recovery (STIR) or Dixon fat suppression, produce images with specific tissues providing little or no contribution to the resulting imaging, which can increase contrast even further [5,33,34].

FDG-PET/CT is a nuclear medicine imaging technique in which localised image intensity is related to the concentration of a glucose analogue and hence, metabolic activity. As tumour cells typically have greater metabolic demands than the corresponding normal cells, the radioactive material is concentrated within the tumour volume. The use of physiological response as an image formation mechanism has shown FDG-PET/CT can provide more current information on disease progression/response following therapy than other radiological techniques. In addition to this, FDG-PET/CT may allow distinction between multiple myeloma and Monoclonal Gammopathy of Unknown Source (MGUS), a related precursor condition [4]. Although other factors for the localised metabolic function such as inflammation and chemo/radiotherapy can produce false negative results, correlation with patient history or an attenuation correction CT scan may improve accuracy. The specific limitation in the application of FDG-PET/CT to Multiple myeloma is system spatial resolution. The large pixel sizes used in FDG-PET/CT, in comparison to other modalities, diminishes the capacity for detection of diffuse disease [7]. The need for both a nuclear medicine (FDG-PET) and radiological (CT) component to most FDG-PET/CT procedures leads to a high effective dose for the procedure, and the 2009 international myeloma working group recommended against the use of FDG-PET/CT for both diagnosis and follow up of myeloma until further studies have been undertaken [5].

Although MIBI SPECT/CT examinations are commonly used for cardiac investigations, the tracer component of the molecule can allow imaging of some invasive cancers to be performed. In the case of plasma cell dyscrasias, such as multiple myeloma, the attachment of the tracer molecule to the infiltrating bone marrow leads to regional increased uptake (or regional concentration of the tracer). MIBI SPECT/CT examinations were found to have a 100% negative predictive value for Myeloma in patients suffering from MGUS and as such may be useful in differential diagnosis between the two diseases [35].

4.4. Direct comparison of planar radiography and CT

The similarity in dosimetry shown here between tin filtration CT and planar radiography for skeletal survey imaging makes either choice equally appropriate when considering only radiation risk. It is also noted that the method employed here for dose calculation does not consider tube current modulation, due to software limitations. Future work using fully customised simulation may be appropriate however, the approach used here ensures doses are calculated conservatively.

Optimisation of any procedure also requires an overall understanding of the examination requested, including consideration of resultant image quality. The image quality of CT is shown to be superior to projection X-ray in a number of significant ways including smaller lesion visualisation as well as higher sensitivity and specificity [5]. The increased soft tissue resolution associated with CT imaging also allows detection of additional disease such as emphysema and lymphadenopathy not possible with projection X-ray [34]. Following acquisition, multi-planar reformatting and three-dimensional orthogonal viewing can be used on images obtained with CT, assisting diagnosis and reporting. Comparison of the image quality from different modalities as applied to multiple myeloma has been reported in the literature, with results showing a minimal difference or recommending EPIC-CT and tin CT [5,25,34,36]. Both CT imaging approaches are not equivalent however, with this work showing EPIC-CT can require 5.7 times the effective dose of tin filtered CT.

In addition to consideration of modality strengths and weaknesses, optimisation of a radiological examination for a patient should consider individual patient needs. Planar radiography requires long examination times, up to 45 min, and over this time the patient is positioned multiple times. In stark contrast, tin-filtration CT studies are performed much quicker, 5–10 min, during which time the patient is comfortably positioned supinely. Given the advanced age profile and likely bone pain of multiple myeloma sufferers, tin filtration CT is likely to be a much more practicable examination [37].

Due to the commonplace nature of projection Radiographic apparatus throughout radiology departments, planar radiography skeletal surveys will remain a useful tool for management of suspected multiple myeloma patients for some time. The large level of demineralisation (up to 50%) before a lytic lesion is visible on radiographic examination limits the sensitivity compared to tin filtration CT, whilst the ubiquitous appearance of myeloma lytic lesions compared to other orthopaedic pathologies on both modalities will limit specificity, providing opportunities for application of other imaging modalities [8].

5. Conclusion

Tin filtration CT provides equivalent or superior diagnostic utility to radiographic skeletal survey [25] at approximately equivalent radiation doses, with better patient comfort and quicker procedure times. Although access to CT is not comparable to planar radiography and the capacity to perform CT examinations using different filtration is limited to select newer scanner models, the increased prevalence and better government subsidy infrastructure of CT compared to MRI, MIBI SPECT/CT and FDG-PET/CT will allow tin filtration CT to continue to fill an important role in improving diagnosis and management of multiple myeloma patients. Selection of appropriate patient specific imaging modality requires consideration of both radiation dosimetry and clinical presentation on a case by case basis, in line with accepted best practice.

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Compliance with ethical standards

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Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors.

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