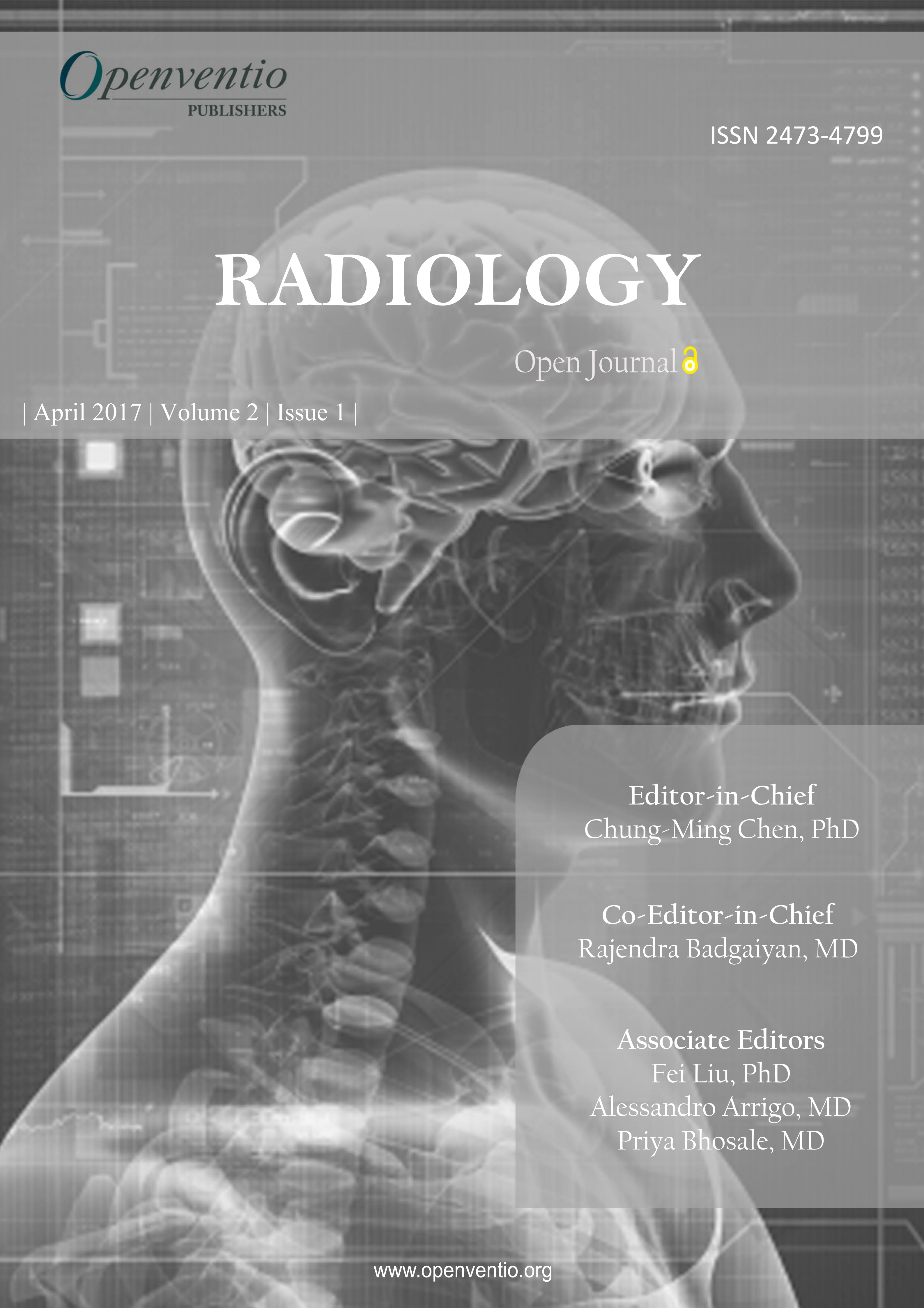

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Editorial

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Update on Limbic Connections in Human Brain: A Possible Closer Relationship Between Brain Processes and Visceral Information

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The limbic system includes cortical and subcortical brain structures involved in several functions, first of all emotional and memory processes and integration. Two key structures of the limbic network are hippocampus and amygdala; their connections with the other brain regions are allowed through a number of white matter pathways, including cingulum, uncinate fasciculus and fornix.[1] All these pathways were studied by means of invasive approaches in animals as well as by means of MRI techniques, e.g. diffusion based tractography. These methods resulted very useful for the non-invasive study, *in vivo*, of these limbic brain connections,[1] as well as to show new possible pathways, e.g. the cerebellar limbic one.[2] Recently, new insights regarding possible limbic functions came from a study conducted by means of advanced tractographic algorithms.[3] The main goal of the latter paper was to investigate subtentorial limbic connections in healthy humans; this was an interesting point, since these connections were previously investigated only in animals by means of viral tracing techniques.[4] These previous studies revealed extensive connections of both amygdala and hippocampus with brainstem nuclei, as well as connections with the periphery of the body through spinal projections.[5,6] By means of constrained spherical deconvolution (CSD)[7] based tractography, Arrigo and colleagues[3] reported and described hippocampal and amygdalar connections with midbrain, pons and bulb as well as connections with cervical spinal cord (Figure 1). These represented novel findings in humans, suggesting that functional speculation based on animals studies might be adopted also in human brain. Amygdalar connections with brainstem were proposed to be related with faster answers to fear stimuli, in order to establish a more efficient alerting mechanism.[8-10] Based on findings provided by animal studies, other authors proposed a role of amygdalar-brainstem pathways in the visceral control as well as in the control of the appetite.[11,12] With respect to hippocampal-brainstem pathways, these were previously reported in animals[13,14]; those results allowed to advance the hypothesis of a larger learning and memory connectivity network, involving also brainstem structures, which might influence the limbic system during memory and learning elaboration.[15] In this context we might advance the hypothesis that information

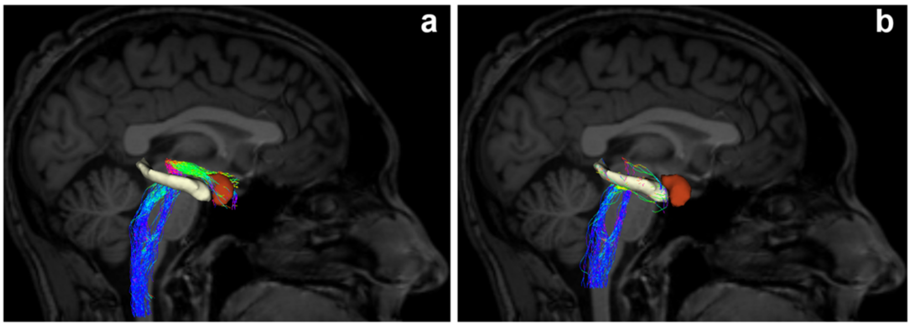

Figure 1: Sagittal view of amygdalar (a) and hippocampal (b) connections with cervical spinal cord. Amygdala and hippocampus are represented by brown and white regions of interest respectively.

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regarding the visceral state in a given moment might influence or take a role in memory and learning processing.[16] Regarding spinal-limbic connections, very little is known about their functional involvement in brain processes. Also in this case, these pathways were supported by previous studies conducted in animals.[5-6] A number of hypotheses might be advanced about the functional meaning of these bundles; an interesting point is related with the possibility that these connections represent a faster way of transmission of nociceptive information and visceral ones, thus making possible faster responses to dangerous or noxious stimuli.

Although, further studies are needed definitely to demonstrate the existence of these connections, i.e. dissection studies, as well as to define their functional meaning, these white matter bundles open new interesting perspectives both in physiological and pathological contexts. Indeed, it might be interesting to study the role of brainstem and the periphery of the body in learning and memory processes, as well as in emotional state integration. Moreover, these pathways might provide further anatomical basis to better define pathophysiological features of a number of psychiatric and syndromic conditions, e.g. bipolar disorder[17,18] and anti-Ma2-associated syndrome.[19,20] In these kind of patients a strong involvement of the limbic system was demonstrated, with concurrent alterations of brainstem nuclei. Furthermore, another interesting future perspective might regard the deeper study of what is known as gut-brain axis, i.e. a bilateral network connecting the periphery of the body both with central and enteric nervous systems.[21] This bidirectional path of connections was described to influence and/or stimulate a number of responses involving nervous, immune and endocrine systems[21]; its alterations was hypothesized to have a role in the pathophysiology of a number of disorders, including functional and inflammatory gastrointestinal disorders, and eating disorders.[16] In particular, with respect to irritable bowel syndrome, previous studies demonstrated alterations of brain functional connectivity, including supra-tentorial limbic circuits.[22,23] Future studies should be conducted in order to understand if an involvement of subtentorial limbic connections occurs in all these contexts.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

DISCLOSURES: None.

REFERENCES

1. Catani M, Dell'acqua F, Thiebaut de Schotten M. A revised limbic system model for memory, emotion and behaviour. *Neurosci Biobehav Rev*. 2013; 37(8): 1724-1737. doi: 10.1016/j.neubiorev.2013.07.001

2. Arrigo A, Mormina E, Anastasi GP, et al. Constrained spherical deconvolution analysis of the limbic network in human, with emphasis on a direct cerebello-limbic pathway. *Front Hum Neurosci*. 2014; 8: 987. doi: 10.3389/fnhum.2014.00987

3. Arrigo A, Mormina EM, Calamuneri A, et al. Amygdalar and hippocampal connections with brainstem and spinal cord: A diffusion MRI study inhuman brain. *Neuroscience*. 2016. pii: S0306-4522(16)30706-0. doi: 10.1016/j.neuroscience.2016.12.016

4. Castle M, Comoli E, Loewy AD. Autonomic brainstem nuclei are linked to the hippocampus. *Neuroscience*. 2005; 134(2): 657-669. doi: 10.1016/j.neuroscience.2005.04.031

5. Giesler GJ Jr, Katter JT, Dado RJ. Direct spinal pathways to the limbic system for nociceptive information. *Trends Neurosci*. 1994; 17(6): 244-250. doi: 10.1016/0166-2236(94)90007-8

6. Newman HM, Stevens RT, Apkarian AV. Direct spinal projections to limbic and striatal areas: Anterograde transport studies from the upper cervical spinal cord and the cervical enlargement in squirrel monkey and rat. *J Comp Neurol*. 1996; 365(4): 640-658. doi: 10.1002/(SICI)1096-9861(19960219)365:4<640::AID-CNE10>3.0.CO;2-L

7. Tournier JD, Calamante F, Connelly A. Robust determination of the fibre orientation distribution in diffusion MRI: Non-negativity constrained super-resolved spherical deconvolution. *Neuroimage*. 2007; 35(4): 1459-1472. doi: 10.1016/j.neuroimage.2007.02.016

8. Usunoff KG, Itzev DE, Rolfs A, Schmitt O, Wree A. Brain stem afferent connections of the amygdala in the rat with special references to a projection from the parabigeminal nucleus: A fluorescent retrograde tracing study. *Anat Embryol (Berl)*. 2006; 211(5): 475-496. doi: 10.1007/s00429-006-0099-8

9. Deboer T, Ross RJ, Morrison AR, Sanford LD. Electrical stimulation of the amygdala increases the amplitude of elicited ponto-

ISSN 2473-0947 Open Journal http://dx.doi.org/10.17140/ROJ-2-e004

geniculo-occipital waves. *Physiol Behav*. 1999; 66(1): 119-124.

10. Liddell BJ, Brown KJ, Kemp AH, et al. A direct brainstem–amygdala–cortical 'alarm' system for subliminal signals of fear. *Neuroimage*. 2005; 24(1): 235-243. doi: 10.1016/j.neuroimage.2004.08.016

11. García-Medina NE, Miranda MI. Nucleus of the solitary tract chemical stimulation induces extracellular norepinephrine release in the lateral and basolateral amygdala. *Brain Stimul*. 2013; 6(2): 198-201. doi: 10.1016/j.brs.2012.03.020

12. Carter ME, Soden ME, Zweifel LS, Palmiter RD. Genetic identification of a neural circuit that suppresses appetite. *Nature*. 2013; 503(7474): 111-114. doi: 10.1038/nature12596

13. Gasbarri A, Packard MG, Campana E, Pacitti C. Anterograde and retrograde tracing of projections from the ventral tegmental area to the hippocampal formation in the rat. *Brain Res Bull*. 1994; 33(4): 445-452. doi: 10.1016/0361-9230(94)90288-7

14. Gasbarri A, Sulli A, Packard MG. The dopaminergic mesencephalic projections to the hippocampal formation in the rat. *Prog Neuropsychopharmacol Biol Psychiatry*. 1997; 21(1): 1-22. doi: 10.1016/S0278-5846(96)00157-1

15. Kirk IJ, McNaughton N. Mapping the differential effects of procaine on frequency and amplitude of reticularly elicited hippocampal rhythmical slow activity. *Hippocampus*. 1993; 3(4): 517-525. doi: 10.1002/hipo.450030411

16. Mayer EA. Gut feelings: the emerging biology of gut-brain communication. *Nat Rev Neurosci*. 2011; 12(8): 453-466. doi: 10.1038/nrn3071

17. Krogias C, Hoffmann K, Eyding J, et al. Evaluation of basal ganglia, brainstem raphe and ventricles in bipolar disorder by transcranial sonography. *Psychiatry Res*. 2011; 194(2): 190-197. doi: 10.1016/j.pscychresns.2011.04.002

18. Sköld M, Källstrand J, Nehlstedt S, et al. Thalamocortical abnormalities in auditory brainstem response patterns distinguish DSM-IV bipolar disorder type I from schizophrenia. *J Affect Disord*. 2014; 169: 105-111. doi: 10.1016/j.jad.2014.08.002

19. Yamamoto T, Tsuji S. Anti-Ma2-associated encephalitis and paraneoplastic limbic encephalitis [In Japanese]. *Brain Nerve*. 2010; 62(8): 838-851. doi: 10.11477/mf.1416100733

20. Waragai M, Chiba A, Uchibori A, Fukushima T, Anno M, Tanaka K. Anti-Ma2 associated paraneoplastic neurological syndrome presenting as encephalitis and progressive muscular atrophy. *J Neurol Neurosurg Psychiatry*. 2006; 77(1): 111-113. doi: 10.1136/jnnp.2005.068775

21. Carabotti M, Scirocco A, Maselli MA, Severi C. The gut-brain axis: Interactions between enteric microbiota, central and enteric nervous systems. *Ann Gastroenterol*. 2015; 28(2): 203-209. Web site. http://annalsgastro.gr/index.php/annalsgastro/article/view/1959/1537. Accessed December 23, 2016

22. Qi R, Liu C, Weng Y, et al. Disturbed interhemispheric functional connectivity rather than structural connectivity in irritable bowel syndrome. *Front Mol Neurosci*. 2016; 9: 141. doi: 10.3389/fnmol.2016.00141

23. Weng Y, Qi R, Liu C, et al. Disrupted functional connectivity density in irritable bowel syndrome patients. *Brain Imaging Behav*. 2016. doi: 10.1007/s11682-016-9653-z

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Short Communication

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The Impact of Industrialization on London Health

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A new multidisciplinary project funded by the City of London Archaeological Trust (CoLAT) Rosemary Green grant will be using the latest imaging techniques on a large sample of archaeological skeletal assemblages from several post-medieval (18th and 19th century) and medieval sites across London as well as other non-metropolitan areas of England for comparison. This project aims to establish for the 1st time a synthetic overview from the physical evidence of how health patterns have changed up to the present day in London and the role that industrialization has played in determining the factors critical to the health of its population, past and present.

One of the most influential changes in our environment, both physical and social, over the past 1000 years has been industrialization, bringing revolutionary wide-spread changes in our material culture, technology, medicine and environment that continue to affect us today. All of these changes have impacted on the health and lifestyles of the modern British population. The industrial period is a pivotal age marking a shift towards increasing longevity and the chronic illnesses associated with aging, as well as a seeming rise in 'man-made' diseases such as cancer. To what extent, then, are these illnesses a product of the industrialized environment we have created? Have these diseases always been present or are they arising as a consequence of our modern, mechanized lifestyles?

This project seeks to identify under-recorded diseases in historic skeletal assemblages (such as metastatic cancers, hyperostosis frontalis interna (HFI) and osteoporosis) using direct radiography (DR) and up-to-date imaging modalities on a large sample of archaeological human skeletal remains, in order to enhance our understanding of the wider impact of industrialization on the health of Londoners in the context of the wider country up to the modern day.

AIMS AND OBJECTIVES

The project will examine the skeletal remains of c. 2,500 individuals to include 1000 adult men and women from industrial period London with the post-medieval population consisting of individuals of all social status. To gauge the impact of industrialization on London itself, the results will be compared to data based on the analysis of a further 500 individuals who lived in the medieval city. The process of industrialization throughout the country was not uniform and comparing the London data to that from non-metropolitan settlements will best capture the effect of living within the highly urbanized environment of the city.

In order to achieve this, the remains of 500 post-medieval individuals in addition to 500 medieval individuals from small towns and cathedral cities will be examined to identify cases of the selected diseases. Archaeological and historical evidence for the nature of the physical surroundings for each site will also be gathered to place the skeletal data into its appropriate environmental context.

The project will enable the much needed research of comparative data on post-medieval assemblages in London, allowing a large scale synthesis that has yet to be produced of how our health has changed as a result of industrialisation in the UK. This will simultaneously

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address a hiatus in our wider palaeopathological and clinical knowledge, currently restricted by a lack of the application of modern imaging techniques to skeletal assemblages.

The project will produce an exciting new resource of digital radiographs, scans and 3D models and will lead to the creation of a large digital archive of human skeletal remains, including virtual 3D models.

METHODS STATEMENT

A total of 18 sites have been identified for radiographic analysis comprising a sample of 1000 post-medieval and 500 medieval London individuals in addition to the remains of 500 medieval and 500 post-medieval non-metropolitan individuals.

We have selected 7 diseases that are often associated with industrialization, urbanization, enriched lifestyles and old age to assess their prevalence over time:

1. HFI: Detected using radiography and computed tomography (CT).
2. Osteoporosis: Detected using radiography.
3. Joint Disease: Detected macroscopically and radiographically.
4. Trauma: Detected macroscopically.
5. Neoplastic disease (cancer): Detected using radiography and CT.
6. Infectious disease (rib lesions): Detected macroscopically.
7. DISH: Detected macroscopically.

Radiographic analysis will be undertaken on strategically selected areas of the skeleton that would allow maximum data to be recorded in a timely and effective manner.

- Crania
- Vertebrae (lumbar)
- Pelvis
- Femora
- 2nd Metacarpal(s)

Radiography of the elements is carried out using a portable direct digital radiographic kit using a Canon CDXI Direct Digital X-ray plate system and Sedecal 4 kW generator (Figures 1 and 2). The process of the radiographed images will follow the guidelines of digital imaging and communications in medicine (DICOM). Recording of radiographic lesions will be undertaken in accordance with Burgener et al[1] and with the interpretative assistance of a radiologist. The crania, vertebrae, femora and hands will undergo radiography in order to assess HFI, osteoporosis and neoplastic disease.

The prevalence of macroscopically observed diseases will be calculated using the Wellcome Osteological Research Database (WORD) and published data. The demographic profile of each assemblage will also be reconstructed to establish the lifespan of men and women. Social status, age, sex and parturition will be taken into account. The data will then be compared to modern clinical data in order to place it in its relevant present day context.

Clinical information and data will be researched *via* online resources, such as the World Health Organisation (WHO) website. Data would be published in an anonymous format to respect the privacy of the deceased and any living relatives. The archaeological evidence for the physical and social environment of each site will be established through desk-top research, so that the skeletal data can be placed into its relevant context. A series

Figure 1: OCU00_18 Positioning of right femur anterior view.

Figure 2: OCU00_18 DICOM image of right femur.

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of maps illustrating the expansion of settlement and industry across the city will also be consulted.

The project is in the initial stages of radiographing individuals from different sites and once completed will then go through all of the radiographic images for analysis and interpretation. The DICOM image below (Figure 3) is of a femur of a female (P4442, SK [969]) from an excavation at Holy Trinity Church, Stratford who died in 1854. The biographical details present for this individual allowed us to obtain a death certificate, which stated the cause of death as 'carcinoma mammae certified'. From the osteological analysis and recording of her skeletal remains there was no macroscopic disease recorded but in the radiograph there appears to be an isolated possible osteolytic lesion.

Figure 3: P4442_969 DICOM image of femur with possible osteolytic lesion.

Collation of the radiographs investigating lesions not visible from macroscopic analysis will be key to the investigations in to the prevalence of diseases that may be present but that are not always visible from gross bony lesions. The advantages of the associated documentary sources for the post-medieval period is having the opportunity of researching parish cause of death and those certified with a death certificate from 1837 onwards in comparison with the osteological analysis. Research projects engaging the use of modern imaging techniques such as DR with archaeological assemblages are proving very fruitful, expanding our knowledge of the diseases present and further substantiating the curated skeletal collections being on-going valuable research assets.

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DISCLOSURE

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCE

1. Burgener A, Coombs K, Butler M. Intracellular ATP and total adenylate concentrations are critical predictors of reovirus productivity from vero cells. *Biotechnol Bioeng.* 2006; 94(4): 667-679. doi: 10.1002/bit.20873

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Giant Peroneal Ganglion Cyst: Imaging and Clinical Findings

Case Report

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ABSTRACT

A ganglion cyst is the cystic lesion originates from the joint capsule or tendon sheath. This lesion is the most common soft tissue tumors of hand, wrist, and foot, and frequently observed in women between 30-50 years. A peroneal ganglion cyst is an uncommon lesion and rarely composes peroneal neuropathic symptoms. We report a 37-year-old man with swelling at the lateral portion of knee below, foot pain, loss of sensation at the lateral portion of left inferior cruris. Ultrasound (US) and magnetic resonance imaging (MRI) findings demonstrated a large cystic lesion in the peroneal muscle, and preliminary diagnosis of peroneal ganglion cyst was proved by cytology. The patient was asymptomatic one month after surgery. There was no evidence of residue or recurrence on US imaging after 6 months.

KEYWORDS: Ganglion cyst; Magnetic resonance imaging (MRI); Peroneus muscle.

INTRODUCTION

Ganglion cyst thought to be the result of myxoid degeneration of joint capsule and tendon sheath connective tissue.[1] This lesion frequently origins from joint capsule, although may also originate from tendon sheath, muscle, nerve, and period. Hand-wrist, foot-ankle are the most common locations respectively.[2] A study on knee magnetic resonance imaging (MRI) revealed 0.76% of the incidence of the peroneal ganglion cysts.[3] Ganglion cysts are the typical lesions although peripheral nerve compression is rare. Peroneal ganglion cysts may lead neuropathy with pain, loss of sensation, weakness on six of the foot ankle and peroneal nerve palsy due to compression of the adjacent peroneal nerve.[4] In this report, we demonstrate a tendon sheath originated peroneal ganglion cyst in large diameter at the proximal musculotendinous junction of peroneus longus muscle proceed to downward in muscle causes severe pain and loss of sensation on cruris.

CASE PRESENTATION

A 37-year-old man applied to a hospital with one-year progressive swelling on the lateral portion of left knee below and pain on the left foot back. In anamnesis, the pain was continuous in last 2 weeks. Physical examination revealed a large, rigid, immobile lesion in the pain location. The patient had loss of sensation on the anterolateral portion of the left cruris below. Ultrasound (US) imaging revealed an 8 cm in length and 3 cm in diameter at its widest point anechogenic cystic lesion spread with a narrow diameter from the left fibula head level to inferior (Figures 1A, 1B and 1C). MRI to characterize the lesion demonstrated an 83×35 mm lesion that was hypointense on T1- and hyperintense on T2-weighted imaging (Figures 2A and 2B). The lesion was originated from the peroneus longus tendon adjacent to lateral part of the left fibula; with a narrow diameter the lesion was proceeded to inferior and the diameter was increased. Preliminary diagnosis of ganglion cyst was held and diagnostic aspiration cytology applied to the patient. The material was serous and in gel consistency; the pathologic result reported as in-

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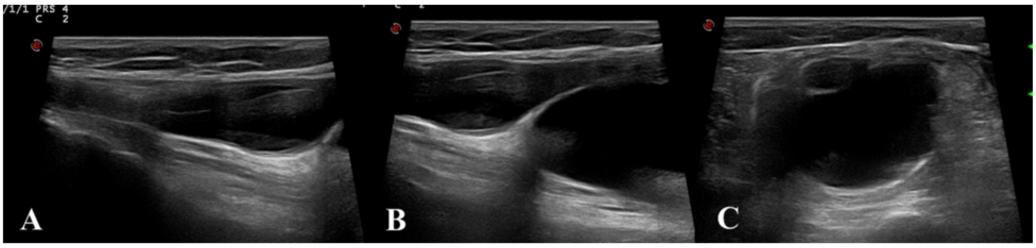
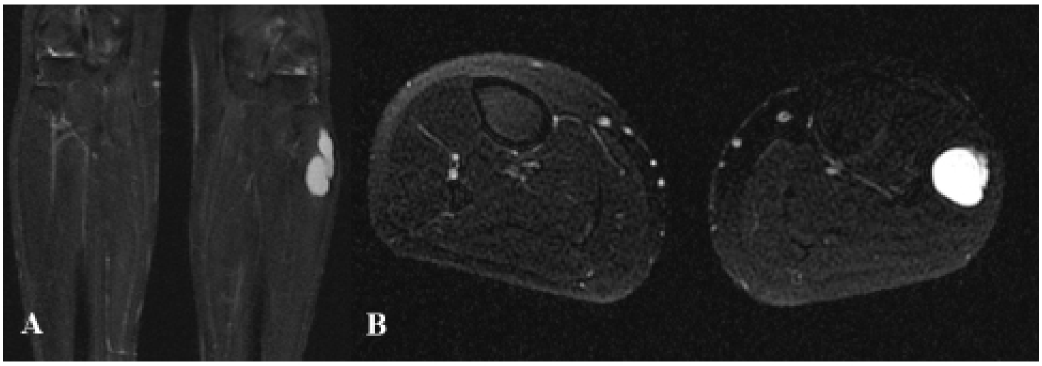


Figures 1: (A and B) Sagittal section on the US. The cyst is forming with a narrow neck and spreads with widening in the muscle. (C) Axial section on US. The inferior component of the cyst demonstrates marked intramuscular trace.



Figures 2: T2-weighted coronal imaging (A) and T2-weighted axial imaging (B) demonstrate hyperintense cystic lesion in the peroneus longus muscle.

tense proteinaceous content. The patient underwent surgery with preliminary diagnosis of a ganglion cyst. Longitudinal incision applied on the lesion trace under the spinal anestesia. The lesion was reached between the musculus peroneus longus muscle fibers. The origin of the lesion observed as the tendinous component of the musculotendinous joint of peroneus longus muscle. The lesion dissected and total excisional biopsy was performed. The area washed with saline solution and after the bleeding control the wound location sutured (Figures 3A and 3B). The ganglion cyst diagnosis was proved by pathology examination. The patient had no pain or loss of sensation on the lateral portion of left lower leg after one month. There was no evidence of residue or recurrence on US imaging after 6 months.

DISCUSSION

Ganglion cysts mostly occur in hand-wrist and foot-angle, respectively.[2] They may establish at any age, although peak incidence is in the thirties. It is more common in women than in men.[5] Our patient was a 37-year-old man.

The exact etiology of the peroneal ganglion cyst is unclear, although trauma, synovial herniation, removal of synovial tissue during embryogenesis are mentioned.[6] Our patient had no trauma history.

It is uncommon to have neurological symptoms due to

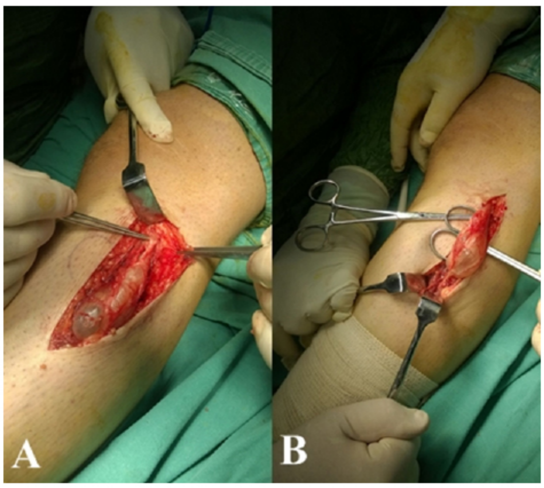


Figure 3: (A and B) Intraoperative appearance of the cyst.

impress of peroneal nerve and roots by a peroneal ganglion cyst, however, severe complications such as drop foot may also occur.[3,7] Our patient had just sensation loss on left lower leg lateral portion without loss of strength. These cysts lead peroneal nerve compression may be peroneal nerve originated ganglion cysts and entitled peroneal intraneural ganglion cyst.[7]

Physical examination and diagnostic tools such as US and MRI may use in the diagnosis of a peroneal ganglion cyst. The US is useful because the technique is inexpensive, noninvasive and easy to implement. A ganglion cyst is a well defined anechogenic cystic lesion on the US. The US can distinct between the robust and cystic components of the lesion, although provides limited information about the relationship with surrounding tissues. The differentiation of ganglion cyst and cystic schwannoma is not always possible in the US. MRI is the selectable modality to determine the extent of the lesion.

A ganglion cyst is typically black on T1- and bright on T2-weighted images of MRI study. After the administration of intravenous (IV) gadolinium, the cyst wall may enhance mildly, although the center of the lesion is unenhanced.

In our patient, we applied US as a primary imaging technique and MRI in next step to demonstrate the relation of the lesion to peripheral structures. Our preliminary diagnosis was the ganglion cyst. Therefore we did not perform IV contrast material. We applied fine needle aspiration cytology for definitive diagnosis before surgery. The aspiration material was intense proteinaceous material on cytology. Histologically, ganglion cysts are filled with viscous gelatinous protein material consisting of hyaluronic acid, albumin, globulin and glucosamine.[8]

Synovial cyst, intramuscular myxoma, cystic degeneration of a schwannoma or neurofibroma, or synovial sarcoma are in the differential diagnosis.[2]

The recent treatment of peroneal ganglion cyst is marginal excision. Also, ligation of cystic peduncle or electrocoagulation has to be a part of surgery to avoid recurrence.[7] In our patient, the peduncle was in large diameter. Therefore ligation or electrocoagulation was unrequired. After 6 months US control imaging demonstrated no evidence of recurrence.

Fine needle aspiration may be an alternative treatment choice in patients with ganglion cyst who hesitate from surgery.[6,7]

CONCLUSION

In conclusion, we aim to emphasize the ganglion cysts usually occur in hand-wrist and foot-ankle and may also establish in peroneal muscle. These cysts may cause peroneal neuropathy symptoms. US and MRI are the reliable tools in diagnosis.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this paper.

CONSENT

The authors have obtained oral consent from the patient for this article.

AUTHORS CONTRİBUTİONS

Özen Ö and Tosun A were involved in radiological imaging of this patient and writing of the case report. Aytekin K and Esenyel CZ were the orthopedic surgeons managing the patient.

REFERENCES

1. Nicholson LT, Freedman HL. Intramuscular dissection of a large ganglion cyst into the gastrocnemius muscle. *Orthopedics.* 2012; 35(7): e1122-e1124. doi: 10.3928/01477447-20120621-36

2. Marano AA, Therattil PJ, Ajibade DV, Datiashvili RO. Ganglion cyst of the peroneus longus. *Eplasty.* 2015; 15: ic20. Web site. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4396405/. Accessed November 17, 2016.

3. Wang EC, Chew FS. Ruptured peroneal ganglion cyst: MRI with surgical correlation. *Radiol Case Rep.* 2015; 2(2): 61-64. doi: 10.2484/rcr.v2i2.35

4. Nikolopoulos D, Safos G, Sergides N, Safos P. Deep peroneal nerve palsy caused by an extraneural ganglion cyst: A rare case. *Case Rep Orthop.* 2015; 2015: 861697. doi: 10.1155/2015/861697

5. Kim YJ, Chae SU, Choi BS, Kim JY, Jo HJ. Intramuscular ganglion of the quadriceps femoris. *Knee Surg Relat Res.* 2013; 25(1): 40-42. doi: 10.5792/ksrr.2013.25.1.40

6. Sever C, Malkoc M, Acar T, Turkmen F, Korkmaz O, Oto O. Ganglion cysts in the lateral portal region of the knee after arthroscopy: Report of two cases. *Autops Case Rep.* 2015; 5(4): 71-76. doi: 10.4322/acr.2015.023

7. Zumrut M, Demirayak M, Kucukapan A. An unusual cause of foot drop: Peroneal extraneural ganglion cyst. *Pak J Med Sci.* 2016; 32(4): 1047-1050. doi: 10.12669/pjms.324.9998

8. Shinawi M, Hicks J, Guillerman RP, et al. Multiple ganglion cysts ('cystic ganglionosis'): An unusual presentation in a child. *Scand J Rheumatol.* 2007; 36(2): 145-148. doi: 10.1080/03009740601089275

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Systematic Review

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The Current Use and Effectiveness of Bismuth Shielding in Computed Tomography: A Systematic Review

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ABSTRACT

Background: The increased use of computed tomography (CT) has raised concerns regarding the radiation dose received by radiosensitive organs. It is important that practical and reliable dose reduction strategies are implemented to reduce patient radiation exposure.
Aims: The purpose of this article is to evaluate the current clinical use and effectiveness of bismuth shielding as a dose reduction technique and assess its impact on image quality, in an attempt to develop a recommendation for dose reduction in CT.
Methods: A systematic review of current literature was conducted using the PubMed and Scopus databases. A total of 50 relevant articles were thoroughly assessed and evaluated.
Results: This review found that whilst bismuth shielding proves to provide significant dose reductions to radiosensitive organs, numerous concerns exist including wasted radiation, reduced image quality and unpredictable results when combined with AEC. Alternative methods such as tube current modulation and iterative reconstruction algorithms can provide equivalent dose savings at superior image quality, without the limitations of bismuth shields.
Conclusion: Until these alternative methods become available in all departments, bismuth shielding remains a viable dose reduction strategy.

KEY WORDS: Computed tomography; Bismuth shielding; Automated exposure control (AEC).

ABBREVIATIONS: CT: Computed Tomography; AAPM: American Association of Physicists in Medicine; AEC: Automated exposure control; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; ASIR: Adaptive Statistical Iterative Reconstruction.

INTRODUCTION

The use of computed tomography (CT) has increased exponentially since its introduction into the clinical setting in 1971.[1] This growth comes as a consequence of numerous technological advances, namely multi-detector capabilities, which have seen CT move to the forefront of medical imaging.[2] Consequently, the expansion of CT has raised concerns regarding radiation exposure and patient-induced health risks.[3] CT contributes to a large portion of the population's radiation exposure, subjecting patients on average to higher doses than its medical imaging counterparts.[4] It is these considerably higher doses that are fuelling concerns regarding the lifetime attributable chance of fatal malignancy, estimated to range from 25 to 33 cases per 100,000 for pelvic, abdominal and chest CT procedures.[5]

Additionally, concerns exist regarding the dose received by radiosensitive organs, specifically the thyroid, breast, gonads and lens of the eye. These organs are made up of radiosensitive cells and are regarded to have a greater stochastic risk of future malignancy with repeated exposure to ionising radiation.[6] It is therefore important that all CT examinations are justified and implement practical and reliable dose reduction techniques.

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In the past, lead shielding was the leading dose reduction strategy used in CT examinations.[7] However, its use was replaced by bismuth shielding, which provided improved opportunities to reduce dose to superficial organs within the field of view.[8] While various studies have proven that lead and bismuth provide equivalent dose reductions[9-11]; bismuth shields are designed for specific superficial organs and have the added benefit of being lightweight and easy to manoeuvre.[8]

Recently, the use of bismuth shields has sparked debate in relation to issues caused during scans. According to the American Association of Physicists in Medicine (AAPM), these issues relate to the degradation of image quality, unpredictable and unreliable results when combined with automated exposure control (AEC) and wasted radiation.[9] The most recent position statement released by the AAPM states that 'other technologies exist that can provide the same level of anterior dose reduction at equivalent or superior image quality that do not have these disadvantages'.[9] These alternative methods include, but are not limited to, organ-based and global tube current modulation and iterative reconstruction techniques, which should be considered and applied when possible.

The purpose of this literature review is to explore current available knowledge in an attempt to determine the most effective technique to reduce dose to radiosensitive organs during CT examinations. The main focus will be placed on evaluating the current clinical use and effectiveness of bismuth shielding. Furthermore, alternative and emerging dose reducing strategies will be investigated in an attempt to help guide contemporary practice.

MATERIALS AND METHODS

A systematic review is a thorough evaluation of the literature and is a key element of evidence-based practice. It involves identifying and selecting relevant studies, appraising their quality and summarising the evidence using explicit methodology, in order to address and provide a non-biased and reliable answer to a formulated question.[12] Systematic reviews are most suited in situations where there is an inconsistency in research methodology causing unreliable results or when a body of research exists; however, findings are not well consolidated. The systematic review aims to organise research findings into themes so future research is focused and valid.[13] There are various recognised approaches that guide the systematic review process.[12-14] The guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were implemented for this review.[14]

Evidence was found by conducting a PubMed and Scopus search to obtain literature regarding the use and effectiveness of bismuth shielding in CT. Key words included: 'Bismuth shielding' OR 'shielding' AND 'CT' OR 'computed tomography' AND dose-reduction. The searches were limited to the English language, with a publication date from 2010 onwards.

This method resulted in a combined total of 102 articles, which were subsequently subject to a thorough screening process, as per the PRISMA guidelines (Figure 1). Titles and abstracts were carefully assessed according to inclusion and exclusion criteria (Table 1). Twenty-three duplicate articles were removed, as well as 29 articles found to be either completely irrelevant or outside the scope of this review, not available or

Figure 1: Flowchart Demonstrating the Screening Process.

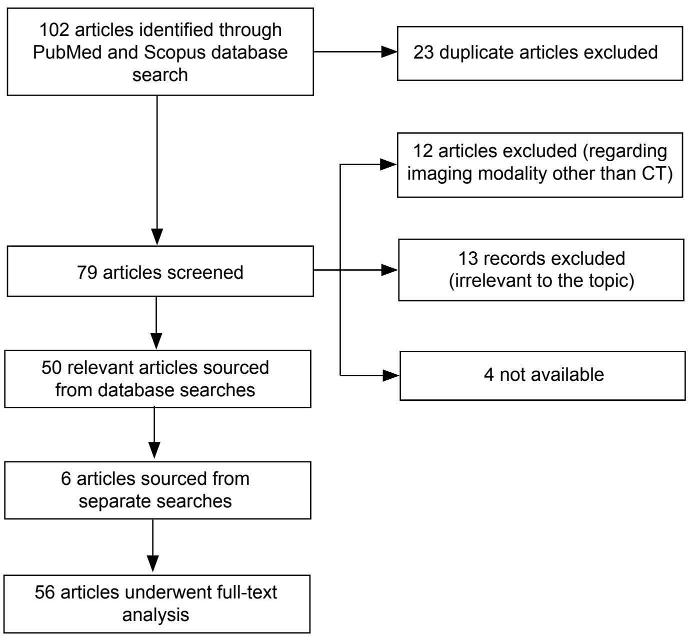

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Table 1: Inclusion and Exclusion Criteria.

Inclusion	Exclusion
• Published between 2010 and present • English language • Peer-reviewed • Reliable source • Studies assessing the current use and effectiveness of bismuth shielding in CT, including at least one of the following: ○ Dose reduction capabilities ○ Impact on image quality • Studies discussing alternative and emerging does reduction strategies in CT • Studies regarding does reduction in CT specifically to radiosensitive organs; particularly the breast, thyroid, gonads and lens of the eye.	• Published before 2010 • Not accessible • Articles discussing: ○ Shielding and other does reduction techniques in medical imaging modalities other than CT ○ Does reduction to others beside the patient (e.g., staff) ○ Room shielding ○ Topics completely irrelevant

regarding another medical imaging modality other than CT.[15]

Additionally, six publications were included that were outside the scope of this search; sourced from recommendations, separate searches and backtracking of articles. Overall, the study sample included 56 relevant articles that were thoroughly assessed and evaluated, to help provide the answers to the clinical question.

RESULTS

There is a well-established and justifiable need to modulate the radiation exposure to radiosensitive organs.[16] For the purpose of this review, four organs: The eye lens, thyroid, breast and gonads, were identified and the effect of bismuth shielding on dose reduction and image quality evaluated.

The image quality parameters discussed in the papers cited in this article include image noise, signal-to-noise ratio, artifacts such as beam hardening. Image noise refers to the random variation of CT numbers and depends on both the quality (beam energy) and quantity (number of photons) of the X-ray beam. Noise has a grainy appearance on images. The signal-to-noise ratio (SNR) on the other hand is a ratio of the true signal (from anatomical structures) to the random quantum mottle (noise).

An artefact is an error on the image that is not related to the anatomy being examined and can mask or mimic clinical characteristics. Two such artefacts that are noted in this paper are:

1. Streak artefacts;
2. Beam hardening artefacts.

While Beam hardening refers to an increase in the mean energy of the X-ray beam as it passes through the patient and appears as shading differences on the image; streak artifacts appear as bright straight lines across the image, and could be caused by the presence of metal in/or on the patients for example. For more details of these artifacts the reader should refer to related articles which will be cited below.

THE EYE LENS

Dose Reduction

CT examinations of the head are among the most frequently performed CT examinations, with a typical radiation dose of 60 mGy.[17] Although the eyes are rarely the area of interest during such examinations, they are often incidentally included within the scan region. This is an area of concern as the eye lens is one of the most radiosensitive organs in the human body.[17-24] According to the International Commission on Radiological Protection (ICRP), the radiation dose threshold for detectable lens opacities resulting in the formation of cataracts is 0.5 Gy.[18,19] Therefore it is prudent that dose reduction strategies are implemented.

There are several studies in the literature that evaluate bismuth shielding as a dose reduction method.[17-25] Where as all studies report a reduction in dose to the eye, the dose savings vary from 20 to 50% depending on the scanner, technique and shield design. Mendes et al[23] conducted a study using an acrylic head phantom to evaluate the dose reduction achieved with and without the application of a bismuth shield covering the eyes. The percentage dose reduction achieved was 36%, verifying the dose reduction capabilities of bismuth eye shields.

Additionally, a study by Wang et al[17] investigated the effect of increasing the thickness of the bismuth shield. This involved scanning an anthropomorphic head phantom using both a single-layer and double-layer of bismuth shielding. The dose reductions achieved were 26.4% and 42.4%, for the single and double-layered shield, respectively. While this study confirms that multiple layers of bismuth increases dose reduction, image quality is compromised in the process, limiting the acceptable thickness and thus, dose reduction capabilities of the shield.

Since it is not possible on many scanners, the literature suggests that when feasible, excluding the eyes from the primary X-ray beam by tilting the gantry along the supraorbital meatal line is the most effective way to reduce dose to the eye lens.[17,18] Studies have reported dose savings of around 80%.[18] Concerns have been raised; however, regarding streak artifacts as a result of beam hardening and partial volume artifacts, as well as reconstruction pitfalls.[18,26,27]

Image Quality

All these shields have proven to provide invaluable dose reductions to the eye lens, their use and effect on image quality remains under debate. Numerous studies have recommended against the use of bismuth shielding due to the presence of streak artifacts extending into the brain, affecting mainly the orbits, inferior frontal lobe and anterior temporal regions.[19,24] In some cases, these artifacts have resulted in images unsuited for diagnostic purposes, with repeat scans required.[19,21]

Furthermore, the application of bismuth causes beam hardening and poor use of information-carrying photons, resulting in increased image noise and inaccurate CT number representation. Several studies have shown a drift in CT numbers between 50 and 65%.[25,26,28]

There are also many studies that support the use of bismuth, suggesting no significant impact on image quality.[19,20,28] Where as these studies agree that streak artifacts disrupt image quality, the majority suggest that by creating a small gap between the eye lens and the shield, artifacts can be reduced to an acceptable diagnostic level.[9,17,19,24,26] Our study by Raissaki et al[24] reduced artifacts to a negligible level by elevating the shield from the eyes using folded gauzes. Distances of 5, 10 and 20 millimeters were evaluated and found to reduce artifacts resulting in only slight decreases to dose reductions. Dose savings of 32%, 30% and 29% at five, 10 and 20 millimeters, respectively were recorded, compared to the 32% dose reduction following direct placement of the shield.

THYROID

Dose Reduction

According to the ICRP the radiosensitive thyroid gland has a tissue-weighting factor of 0.04, meaning an increased risk of stochastic injury and future malignancy with exposure to ionising radiation.[23] Although rarely an organ of interest, the thyroid gland is often incidentally exposed to the primary X-ray beam during neck and thorax CT examinations. Therefore, because of its radiosensitive nature and frequent radiation exposure it is important that the dose to the thyroid is limited.

Catuzzo et al[20] conducted a study to investigate the dose reduction capabilities of bismuth thyroid shields. This involved dose measurements calculated using thermoluminescent dosimeters on both phantoms and patients, with and without bismuth shielding. They recorded 32.16% and 30% 10% dose savings on phantoms and patients, respectively. These measurements correspond well with several other studies in the literature that report reductions between 25 and 40%.[6,23,30,31]

Another study performed by Inkoom et al[32] explored the effect of combining bismuth shielding with AEC. The authors examined the effect that bismuth shielding, AEC and a combination of the both had on the dose to four pediatric anthropomorphic phantoms. Dose reductions increased from 25% with bismuth alone, to 62% when combined with AEC. Use of AEC with bismuth must be considered carefully; however, due to unpredictable and unreliable effect on image quality.

Image Quality

As stated earlier, the use of bismuth shielding in CT is associated with the presence of beam hardening and streak artifacts.[32] While some studies disprove of the use of bismuth in thyroid CT examinations because of the degradation of image quality caused by such artifacts,[30,31] others conclude no quantitative or qualitative impact on image quality.[6,21,31]

A key issue associated with thyroid shields is the negative impact on CT attenuation values. Our study by Lee et al[31] recorded increases in CT numbers in the superficial neck muscles. These results suggest the use of bismuth shields must be carefully considered as they may degrade the diagnostic accuracy of an image.

BREAST

Dose Reduction

Radiation protection of the breasts in female patients during CT examinations is important for two main reasons. Firstly, female glandular breast tissue has increased radiosensitivity, with an associated tissue-weighting factor specified by the ICRP of 0.12.[5,19,33] Secondly, the breast is often incidentally exposed to large doses of radiation during CT procedures, even though they are rarely the area of interest.[34,35] Although routine chest CT scanning contributes to the majority of breast irradiation, numerous examinations are of concern. For example, CT pulmonary angiography can result in a mean glandular dose between 20-60 mGy, where as the inferior aspect of the breast can receive 10-20 mGy during abdominal CT.[5] Therefore because of the breasts overall projected radiosensitivity and high incidence of irradiation, reliable and practical dose reduction techniques must be routinely implemented.

The vast majority of publications relating to the use of bismuth shields in CT confirm its ability to produce considerable

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dose reductions to the breasts. These studies suggest dose savings ranging from 20 to 60%, depending on patient type, scanner, shield design and protocol used.[34-40] Catuzzo et al[20] reported a breast dose reduction in female patients during a routine chest CT of 41%, Abadi et al[42] recorded a 38.4% reduction during CT angiography scans of a phantom and Small et al[43] produced dose savings of 62% during cardiac CT scanning when combining the use of bismuth shielding with ECG-gated tube current modulation. Additionally, there are numerous studies that report dose reductions to the breast of around 30% on paediatric phantoms.[22,28,37,47]

Image Quality

The widespread use of bismuth breast shielding is limited by many conflicting ideas regarding image quality. There are various studies that advocate the use of bismuth shielding for breast dose reduction suggesting acceptable deterioration in image quality with no impact on interpretability.[5,20] One study performed by Einstein et al[44] investigated the use of bismuth shields during CT coronary angiography examinations and observed no streak artifacts, whilst a separate study by Colletti[5] reported no significant impact on signal-to-noise ratio or image quality.

These findings however, are contrasted against several studies in the literature that are against the use of bismuth breast shields.[5,35,46] Several of these studies report significant increases in image noise.[5,35,41] Wang et al[39] showed image noise in both the heart and lung, with increasing noise closer to the shield, where as the study by Einstein et al[44] showed increased noise affecting coronary artery visualisation. Investigators have also reported the presence of undesirable streak and beam hardening artifacts.[19,30] Furthermore, evidence exists regarding changes in CT numbers within the heart and lung regions.[39,44,46] These studies suggest that such a drift in CT numbers has adverse effects on plaque characterisation and coronary artery calcium scoring.

GONADS

Dose Reduction

The gonads are a radiosensitive organ not commonly targeted during CT imaging; however, they are exposed to radiation as a consequence of their anatomical location.[48] Despite this, there is very little research into the use of bismuth shielding to protect the gonads. Sancaktutar et al[49] recently performed a study on two hundred male patients. They investigated the dose savings that resulted when using 2 bismuth-lined gloves to protect the scrotum during abdomniopelvic CT examinations. This bismuth testes shield produced dose savings of 90.2%. Additionally, an older study using bismuth shielding on a phantom, resulted in a mean dose reduction of 50.5%.[50] Whilst these studies confirm the dose saving capabilities of bismuth, further research is recommended to verify these findings and investigate the effect on image quality.

The majority of CT dose reduction research in relation to protecting the gonads from ionising radiation is in relation to 'out-of-plane' lead shielding. This refers to the application of conventional lead aprons or custom-designed lead shields, to the pelvic region during CT examinations where the gonads remain outside the scan region. Several studies have investigated such techniques during CT examinations of the chest.[29,51] These studies yielded dose savings between 70 and 90%. This technique involves the risk of causing severe artifacts if the lead is placed within the scan plane, the recommendation to protect anatomy lying outside the scan plane from scatter radiation using lead has proven viable.

DISCUSSION

The Argument for Bismuth Shields

Bismuth shields are commercially available, relatively inexpensive, require little training to implement correctly, are lightweight causing minimal discomfort and are simple and convenient to use.[20,28,32,52] They function independently and thus can be used on all CT scanners from differing manufactures.[35] Furthermore, they are associated with making the patient feel comfortable and confident when being exposed to ionising radiation.[16]

The primary argument supporting the use of bismuth shields in CT is their unquestionable ability to reduce dose to superficial radiosensitive organs. The literature reveals a consistent agreement regarding their effectiveness, with one study by Akhlaghi et al[48] showing that even small thicknesses of bismuth result in significant dose reductions.

Further support for the use of bismuth shields comes from numerous statements from professionals suggesting bismuth shielding has a negligible effect on image quality.[20,40,46,48,53] The majority of these reports come from studies that offset the shield from the patient. One study by Inkoom et al[32] showed noise reductions of 69%, 87% and 92% when separating the shield from the patient by 1, 2 and 3 cm, respectively, using a cotton spacer. Other studies report that shielding causes negative impacts on image quality, these effects only occur in the superficial tissues, which are rarely the area of interest.[16,20,48]

Additionally, Samei[16] claims that bismuth shielding allows controlled dose and noise manipulation to occur within a limited region of the body and thus allows effective dose reductions to organs not commonly of interest and thus where a tolerable enhancement of noise is permitted at no compromise to the overall diagnostic quality of the image. All of these claims supporting the use of bismuth shielding in CT coincide with the limited evidence in literature reporting a missed diagnosis as a result of bismuth.[52]

The Argument Against Bismuth Shields

Despite the dose reduction capabilities of bismuth shields, there are numerous studies that discourage their use.[5,17,18,29,39,52] According to several publications[5,34,54] bismuth shields are costly,

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time consuming and increase the risk of patient contamination if the shields are used multiple times without appropriate infection control procedures. Furthermore, in reference to the position statement issued by the AAPM, there are three main disadvantages with the use of bismuth shields: Adverse effects on image quality, unpredictable and undesirable results when combined with AEC and wasted radiation.

Bismuth shields are associated with disrupting image quality and CT number accuracy. Significant increases in image noise have been reported in superficial tissues, decreasing with depth into the patient.[33,55] Whilst numerous studies have suggested introducing a space between the shield and patient eliminates this effect, one study by McCollough et al[43] on the effect of bismuth breast shields, showed an increase in noise within the thorax, even with a 6 cm offset.

Further, effects on image quality result from beam hardening and streak artifacts caused by the attenuation properties of the shield.[32,33] In numerous studies, the presence of these artifacts has resulted in a negative impact on the accuracy and quantitative measurement of CT numbers.[16,29,52] One study by Goldin et al[56] quantitatively analyzed the attenuation effect of bismuth shielding on a solid water phantom during CT chest scans. They reported a drift in CT number of up to 50.6 Hounsfield Units (HU) near the surface of the phantom, with changes decreasing with increasing distance from the shield. This effect could lead to possible mischaracterization and misdiagnosis of a variety of pathologies, strengthening the argument against bismuth shielding, especially when quantitative assessment of CT numbers is critical for diagnosis.

A second concern is associated with the use of bismuth shielding in conjunction with AEC. AEC adaptively modifies the scanners output based on patient attenuation, increasing x-ray flux when encountering an area with higher attenuation.[16] As the combination of bismuth shielding and AEC has been reported in various studies to improve dose reductions,[2,6,43] the technique is associated with unpredictable and undesirable effects on dose and image quality when used inaccurately.[9]

The majority of CT scanners use AEC algorithms based on the scout image acquired prior to the CT acquisition.[57] If the shield is placed on before the scout then the system will increase the tube current based on increased attenuation from the shield, meaning a possible increase in both organ and total patient dose.[16] A study by Colletti et al,[5] revealed placing the shield before the scout during a chest CT, increased dose to the central breast by 29% and dose to the total patient by 20%. Additionally, the use of bismuth shields in CT systems where the AEC algorithm is modulated during the CT scan is strongly discouraged as the system continuously increases tube current in response the shield, counteracting its intended benefit.[52]

Finally, the use of bismuth shielding is considered to be ineffective for use in radiation protection of patients.[18,33,57] Bismuth shields attenuate the anteriorly orientated X-ray beam, they also attenuate the posteriorly orientated beam that has already traversed through patient.[16,17] This means that the information-carrying photons that have entered posteriorly and have deposited dose in the patient, are attenuated by the shield and are unable to reach the detector to contribute to image formation. DeMaio et al[29] reported a loss of data up to 50%.

Alternative Techniques

With so many conflicting ideas concerning the use of bismuth shields, emphasis in current research has been placed on alternative dose reduction strategies that attempt to optimise both dose and image quality during CT procedures. This trend is in line with the current AAPM statement suggesting 'other technologies exist that can provide the same level of anterior dose reduction at equivalent or superior image quality that do not have these disadvantages'.[9] The most promising alternative techniques include organ-based tube current modulation (OBTCM), global tube current modulation and iterative reconstruction algorithms.

Organ-Based Tube Current Modulation

This technique involves reducing the tube current during a 120° radial arc over the anterior aspect of the patient, and increasing the tube current within the remaining 240-degree arc. This modulation keeps the overall radiation dose constant while reducing direct exposure to anterior radiosensitive organs.[3] One study by Nikupaavo et al[6] used OBTCM on phantoms to reduce dose to the lens during head CT and reported 32% dose reductions. Similarly, Kim et al[34] reported dose reductions of 20.8% to the superficial breast tissue and 18.8% to the deep portion of the breasts, using OBTCM on female patients undergoing routine chest CT examinations.

Despite these dose saving capabilities however, OBTCM has been shown to increase dose to posteriorly and laterally located structures.[58] Research by Hoang et al[6] reported dose increases of 29% to the upper lungs and 15-20% to spinal bone marrow, Also noting smaller increases in dose to the posterior brain. With such varying influences in dose, the use of OBTCM must be carefully considered.

Additionally, it is important to consider the image quality effects of OBTCM. The majority of studies report no degradation of image quality,[6,29] with one study by Wang et al[17] reporting no streak artifacts and no significant impact on image noise or CT numbers. Despite this support however there are several reports identifying an increase in image noise. Nikupaavo et al[6] described increases in image noise of 30%, 29% and 12% in the posterior, central and anterior regions of the brain respectively, when using OBTCM during routine head CT scans.

There are also many additional concerns with the use of OBTCM. Kim et al[34] raised concerns relating to the influence of patient anatomy, stating that in patients with larger breasts a portion of the breast tissue may fall within the lateral scan region, where an increased tube current would result in an increased

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amount of dose to the breast. Furthermore, if the patient is positioned off-center than radiosensitive organs could potentially receive more dose from the increased tube current portion of the rotation.[40,59] Lai et al[59] reported an increase in dose of 18% to the eye lens and 50% to the breast dose when positioning a phantom off-center during CT scans using OBTCM.

Global Tube Current Modulation

This technique involves reducing the tube current over the entire 360-degree rotation, decreasing the radiation dose not only to radiosensitive organs, but also to the entire scan region.[5,34] Compared to bismuth shielding, globally reducing the tube current causes equivalent does reductions to radiosensitive organs,[17,39,45] with the cost of slight decreases in image quality. This occurs as reducing the tube current inevitably leads to an increase in image noise.[57] Numerous studies, such as that performed by Wang et al[17] recorded increased noise within the anterior and central areas of the brain, along with minor but significant increases in noise to the posterior regions, when globally reducing the tube current during routine head CT scans. Despite this, reports suggest no streak artifacts or changes in CT numbers.[17,34]

Additionally, globally reducing the tube current during low-dose CT examinations should be avoided, as further reducing the tube current will increase the risk of producing diagnostically unsuited images.[34] Overall, if a slight increase in image noise is acceptable for diagnosis, than globally reducing the tube current is superior to bismuth as it produces similar dose savings with no impact on CT numbers and no additional steps required to position and clean the shield.

Iterative Reconstruction Algorithms

Adaptive statistical iterative reconstruction (ASIR) is an example of one such iterative reconstruction algorithm. It is a complex and computationally demanding method of image reconstruction. It uses recent advanced mathematical models to reduce noise, thereby allowing high quality image acquisition at a lower tube current, thus enabling significant reductions in dose.[3,8,37] There have been numerous studies recently aimed at evaluating the effectiveness of ASiR as a dose reduction method. One study by Mathieu and Cody[35] used ASiR on a phantom during a routine chest CT and noted dose reductions ranging from 30% to 44%. These results are consistent with similar studies in the literature reporting dose reductions of 32-65%.[37]

Furthermore, the majority of studies agree in regards to the effects of ASiR on image quality. A study by Nikupaavo et al[18] found ASiR reduced noise by approximately 20% and had no significant effects on CT numbers. Additionally, Kim et al[60] investigated the effect of combining ASiR with the use of in-plane bismuth shielding and noted both reduced radiation dose and reduced bismuth induced noise increases. In general, ASiR has recently become commercially available and although comes at a financial cost due to software and hardware upgrades, is a promising alternative to the traditional filtered back projection that has the potential to create significant dose savings.[37]

CONCLUSIONS

This manuscript performed a systematic review of current literature to evaluate the use and effectiveness of bismuth shielding as a dose reduction method in contemporary CT practice. The analysis revealed that since bismuth shielding proves to provide significant dose reductions to radiosensitive organs, conflicting ideas exist regarding its ability to produce consistent diagnostic images. These findings are consistent with the current AAPM statement suggesting that alternative methods such as tube current modulation and iterative reconstruction algorithms can provide equivalent dose savings to radiosensitive organs at superior image quality, without the disadvantages of bismuth shields.

Where as numerous studies exist regarding these alternative methods, further research aimed at assessing their use and effectiveness is required in order to encourage their widespread application. Currently, tube current modulation and iterative techniques are not available on all CT scanners. Although these techniques should be considered and applied when possible, until further research and standardised equipment becomes available in all departments, in-plane bismuth shielding remains a viable option.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

1. Sarma C, Hilbrum ME, Conner KE, Stevens SM, Woller SC, Elliott CG. Radiation and chest CT scan examinations: What do we know? *Chest.* 2012; 142(3): 750-760. doi: 10.1378/chest.11-2863

2. Lee K, Lee W, Lee J, Lee B, Oh G. Dose reduction and image quality assessment in MDCT using AEC (D-DOM & Z-DOME) and in-plane bismuth shielding. *Radiat Prot Dosimetry*. 2010; 141(2): 162-167. doi: 10.1093/rpd/ncq159

3. Gunn ML, Kohr JR. State of the art: Technologies for computed tomography dose reduction. *Emerg Radiol*. 2010; 17(3): 209-218.

4. Radiological Society of North America. Radiation dose in x-ray and CT exams. 2015. Web site. http://www.radiologyinfo.org/en/pdf/safety-xray.pdf. Accessed October 23, 2016.

5. Colletti PM, Micheli OA, Lee OA. To shield or not to shield: Application of bismuth shields. *AJR*. 2013; 200(3): 502-507 doi: 10.2214/AJR.12.9997

6. Hoang JK, Yoshizumi TT, Ngyuen GG, et al. Organ-based

ISSN 2473-0947
http://dx.doi.org/10.17140/ROJ-2-113

dose current modulation and thyroid shields: Techniques of radiation dose reduction for neck CT. *AJR*. 2012; 198(5): 1132-1138. doi: 10.2214/AJR.11.7445

7. Lincoln L, Bernland M. To shield or not to shield? Society of computed tomography and magnetic resonance. 2012. Web site. http://www.scbtmr.org/Portals/9/Meetings/2012/Symposium/To%20Shield%20or%20Not%20to%20Shield-Berland.pdf. Accessed October 23, 2016.

8. Chatterson LC, Leswick DA, Fladeland DA, Hunt MM, Webster ST. Lead versus bismuth-antimony shield for fetal dose reduction at different gestational ages at CT pulmonary angiography. *Radiology*. 2011; 260(2): 560-570. doi: 10.1148/radiol.11101575

9. American Association of Physicists in Medicine. Position statement on the use of bismuth shielding for the purpose of dose reduction in CT scanning. AAPM Board of Directors. Web site. http://citeseerx.ist.psu.edu/viewdoc/summary?doi=10.1.1.231.4997. Updated Feb 2012, Cited Feb 16, 2016. Accessed October 23, 2016.

10. Chang KH, Lee W, Choo DM, Lee CS, Kim Y. Dose reduction in CT using bismuth shielding: Measurements and monte Carlo simulations. *Radiat Prot Dosimetry*. 2009; 138(4): 382-388. doi: 10.1093/rpd/ncp278

11. Ngaile JE, Uiso C, Msaki P, Kazema, R. Use of lead shields for radiation protection of superficial organs in patients undergoing head CT examinations. *Radiol Prot Dosimetry*. 2008; 130(4): 490-498. doi: 10.1093/rpd/ncn095

12. Higgins J, Green S. Cochrane handbook for systematic reviews of interventions. 2016. Web site. http://www.cochrane-handbook.org. Accessed October 23, 2016.

13. Fleming PS, Koletsi D, Pandis N. Blinded by PRISMA: Are systemic reviewers focusing on PRISMA and ignoring other guidelines? *PLoS ONE*. 2014; 9(5): e96407. doi: 10.1371/journal.pone.0096407

14. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: A proposal for reporting. *JAMA*. 2000; 283(15): 2008-2012. doi: 10.1001/jama.283.15.2008

15. Khan KS, Kunz R, Kleijnen J, Antes, G. Five steps to conducting a systematic review. *J R Soc Med*. 2003; 96(3): 118-121.

16. Samei E. Pros and cons of organ shielding for CT imaging. *Pediatr Radiol*. 2014; 44(3): 495-500. doi: 10.1007/s00247-014-3084-z

17. Wang J, Duan X, Christner JA, Leng S, Grant KL, McCollough CH. Bismuth shielding, organ-based tube current modulation and global reduction of tube current for dose reduction to the eye at head CT. *Radiology.* 2012; 262(1): 191-198. doi: 10.1148/radiol.11110470

18. Nikupaavo U, Kaasalainen T, Reijonen V, Ahonen SM, Kortesniemi M. Lens dose in routine head CT: Comparison of different optimization methods with anthropomorphic phantoms. *AJR*. 2015; 204(1): 117-123. doi: 10.2214/AJR.14.12763

19. Huggett J, Mukonoweshuro W, Loader R. A phantom-based evaluation of three commercially available patient organ shields for computed tomography x-ray examinations in diagnostic radiology. *Radiat Prot Dosimetry*. 2013; 155(2): 161-168. doi: 10.1093/rpd/ncs327

20. Catuzzo, P, Aimonetto, S, Fanelli, G, et al. Dose reduction in multi-slice CT by means of bismuth shields: Results of in vivo measurements and computed evaluation. *Radiol Med*. 2010; 115(1): 152-169. doi: 10.1007/s11547-009-0469-4

21. Gbelcona L, Nikodemova D, Horathova M. Dose reduction using bismuth shielding during pediatric CT examinations in Slovakia. *Radiol Prot Dosimetry*. 2011; 147(1-2): 160-163. doi: 10.1093/rpd/ncr336

22. Morford K, Watts LK. Bismuth shielding during CT exams: A literature review. *Radiol Manage*. 2012; 34(3): 45-47.

23. Mendes M, Costa F, Figueira C, Madeira P, Teles P, Vaz, P. Assessment of patient dose reduction by bismuth shielding in CT using measurements, GEANT4 and MCNPZ simulations. *Radiol Prot Dosimetry*. 2015; 165(1-4): 175-181. doi: 10.1093/rpd/ncv059

24. Raissaki M, Perisinakis K, Damilakis J, Gourtsoyiannis N. Eye-lens bismuth shielding in pediatric head CT: Artifact evaluation and reduction. *Pediatr Radiol*. 2010; 40(11): 1748-1754. doi: 10.1007/s00247-010-1715-6

25. Seoung YH. Evaluation of radiation dose reduction during CT scans using oxide bismuth and nano-barium sulfate shields. *JKPS*. 2015; 67(1): 1-6. Web site. https://arxiv.org/abs/1503.03702. Accessed October 23, 2016.

26. Lai CW, Cheung HY, Chan TP, Wong TH. Reducing the radiation dose to the eyes lens region during CT brain examination: The potential beneficial effect of the combined use of bolus and a bismuth shield. *Radioprotection*. 2015; 50(3): 195-201. doi: 10.1051/radiopro/2015003

27. Liebmann M, Lullau T, Kluge A, Poppe B, Von Boetticher H. Patient radiation protection covers for head CT scans: A clinical evaluation of their effectiveness. *Rofo*. 2014; 186(11): 1022-1027. doi: 10.1055/s-0034-1366279

28. Kim S, Frush DP, Yoshizumi TT. Bismuth shielding in CT:

Support for use in children. *Pediatr Radiol*. 2010; 40(11): 1739-1743. doi: 10.1007/s00247-010-1807-3

29. DeMaio DN, Turk J, Palmer E. Shielding in computed tomography: An update. *Radiol Technol*. 2014; 85(5): 563-569. Web site. http://www.radiologictechnology.org/content/85/5/563.extract. Accessed October 23, 2016.

30. Antypas EJ, Sokhandon F, Farah M, et al. A comprehensive approach to CT radiation dose reduction: One institution's experience. *AJR*. 2011; 197(4): 935-940. doi: 10.2214/AJR.11.6460

31. Lee Y, Park ET, Cho P, et al. Comparative analysis of radiation dose and image quality between thyroid shielding and unshielding during CT examination of the neck. *AJR*. 2011; 196(3): 611-615. doi: 10.2214/AJR.10.4955

32. Inkoom S, Papadakis A, Raissaki M, et al. Pediatric neck multi-detector computed tomography: The effect of bismuth shielding on thyroid dose and image quality. *Radiat Prot Dosimetry*. 2016; pii: ncw007. doi: 10.1093/rpd/ncw007

33. Geleijns J, Wang J, McCollough CH. The use of breast shielding for dose reduction in pediatric CT: Arguments against the proposition. *Pediatr Radiol*. 2010; 40(11): 1744-1747. doi: 10.1007/s00247-010-1808-2

34. Kim YK, Sung YM, Choi JH, Kim EY, Kim HS. Reduced radiation exposure of the female breast during low-dose chest CT using organ-based tube current modulation and a bismuth shield: Comparison of image quality and radiation dose. *AJR*. 2013; 200(3): 537-544. doi: 10.2214/AJR.12.9237

35. Mathieu KD, Cody DD. Partial arc beam filtration: A novel approach to reducing CT breast radiation dose. *AJR*. 2013; 200(3): 601-607. doi: 10.2214/AJR.12.8771

36. Rupcich F, Badal A, Popescu LM, Kyprianou I, Schmidt TG. Reducing radiation dose to the female breast during CT coronary angiography: A simulation study comparing breast shielding, angular tube current modulation, reduced kV, and partial angle protocols using unknown location signal detectability metric. *Med Phys*. 2013; 40(8): 081921. doi: 10.1118/1.4816302

37. Coakley FV, Gould R, Yeh BM, Arenson RL. CT radiation dose: What can you do right now in your practice? *AJR*. 2011; 196(3): 619-625. doi: 10.2214/AJR.10.5043

38. Hulten E, Devine P, Welch T, et al. Comparison of coronary CT angiography image quality with and without breast shields. *AJR*. 2013; 200(3): 529-536. doi: 10.2214/AJR.11.8302

39. Wang J, Duan X, Christner JA, Leng S, Yu L, McCollough CH. Radiation dose reduction to the breast in thoracic CT: Comparison of bismuth shielding, organ-based tube current modulation and use of a globally decreased tube current. *Med Phys*. 2011; 38(11): 6084-6092. doi: 10.1118/1.3651489

40. Zhang J, Oates EM. CT bismuth breast shielding: Is it time to make your own decision. *AJR*. 2012; 9(12): 856-858. doi: 10.1016/j.jacr.2012.05.008

41. Revel MP, Audureau E, Benzakoun J, Lederlin M, Chabi ML, Rousset P. Breast dose reduction options during thoracic CT: Influence of breast thickness. *AJR*. 2015; 204(4): 421-428. doi: 10.2214/AJR.14.13255

42. Abadi S, Mehrez H, Ursani A, Parker M, Paul N. Direct quantification of breast dose during coronary CT angiography and evaluation of dose reduction strategies. *AJR*. 2011; 196(2): W152-W158. doi: 10.2214/AJR.10.4626

43. Small G, Kazmi M, DeKemp R, Chow B. Established and emerging dose reduction methods in cardiac computed tomography. *J Nucl Cardiol*. 2011; 18(4): 570-579. doi: 10.1007/s12350-011-9400-1

44. Einstein AJ, Elliston CD, Groves DW, et al. Effect of bismuth breast shielding on radiation dose and image quality in coronary CT angiography. *J Nucl Cardiol*. 2011; 19(1): 100-108. doi: 10.1007/s12350-011-9473-x

45. Rupcich F, Kyrianou I, Badal A, Schmidt TG. Energy deposition in the breast during CT scanning: Quantification and implications for dose reduction. *SPIE Medical Imaging (796128)*. 2011. doi: 10.1117/12.878861

46. Servaes S, Zhu X. The effects of bismuth breast shields in conjunction with automatic tube current modulation in CT imaging. *Pediatr Radiol*. 2013; 43(10): 1287-1294. doi: 10.1007/s00247-013-2687-0

47. Lai NK, Liao YL, Chen TR, Tyan YS. Real-time estimation of dose reduction for pediatric CT using bismuth shielding. 2011; 46(12): 2039-2043.

48. Akhlaghi P, Miri-Hakimabad H, Rafat-Motavalli L. Effects of shielding the radiosensitive superficial organs of ORNL pediatric phantoms on dose reduction in computed tomography. *J Med Phys*. 2014; 39(4): 238-246. doi: 10.4103/0971-6203.144490

49. Sancaktutar AA, Bozkurt Y, Onder H, et al. A new practical model of testes shield. The effectiveness during abdomniopelvic computed tomography. *J Androl*. 2012; 35(5): 984-989. doi: 10.2164/jandrol.111.015560

50. Hopper AD, King SH, Lobell ME, TenHave TR, Weaver JS. The breast: In-plane x-ray protection during diagnostic thoracic CT – Shielding with bismuth radioprotective garments. *Radiology*. 1997; 205(3): 853-858. doi: 10.1148/radiology.205.3.9393547

51. Iball GR, Brettle DS. Organ and effective dose reduction

ISSN 2473-0947

http://dx.doi.org/10.17140/ROJ-2-113

in adult chest CT using abdominal lead shielding. *Br J Radiol*. 2011; 84(1007): 1020-1026. doi: 10.1259/bjr/53865832

52. McCollough CH, Wang J, Gould RG, Orton CG. Point/Counterpoint: The use of bismuth shields for CT should be discouraged. *Med Phys*. 2012; 39(5): 2321-2323. doi: 10.1118/1.3681014

53. Curtis JR. Computed tomography shielding methods: A literature review. *Radiol Technol*. 2010; 81(5): 428-436. Web site. http://www.radiologictechnology.org/content/81/5/428.short. Accessed October 23, 2016.

54. Dobbs M, Ahmed R, Patrick LE. Bismuth breast and thyroid shield implementation for pediatric CT. *Radiol Manage*. 2011; 33(1): 18-22. Web site. http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.675.7766&rep=rep1&type=pdf. Accessed

55. Costello JE, Cecava ND, Tucker JE, Bau JL. CT radiation dose: Current controversies and dose reduction strategies. *AJR*. 2013; 201(6): 1283-1290. doi: 10.2214/AJR.12.9720

56. Goldin D, Emerson S, Farah MC, et al. Shielding artificially increases the attenuation of water: Study of CT gradient attenuation induced by shielding (CT GAINS). *Acad Radiol*. 2013; 20(2): 231-237. doi: 10.2214/AJR.12.9720

57. Correia PD, Granzotti CR, Santos Y, da S, Brochi MA, de Azevedo-Marques PM. Characterization of a lead breast shielding for dose reduction in computed tomography. *Radiol Bras*. 2014; 47(4): 223-227. doi: 10.1590/0100-3984.2013.1861

58. Matsubara K, Sugai M, Toyodoa A, et al. Assessment of an organobased tube current modulation in thoracic computed tomography. *J Appl Clin Med Phys*. 2012; 13(2): 148-157. doi: 10.1002/acm2.12024

59. Lai NK, Chen TR, Tyan, YS, Tsai HY. Off-center effect on dose reduction to anterior surfaces with organ-based tube-current modulation. *Rad Meas*. 2013; 59: 155-159.

60. Kim MS, Choi J, Kim SY, Kweon DC. Adaptive statistical iterative reconstruction and bismuth shielding for evaluation of dose reduction to the eye and image quality during head CT. *J Korean Phys Soc*. 2014; 64(6): 923-928. doi: 10.3938/jkps.64.923

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Research

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Evaluation of Whole Body Diffusion-Weighted Imaging in the Staging and Treatment Response of Lymphoma Compared With Fluoride-Oxyglucose (FDG) PET/CT as a Reference Standard

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ABSTRACT

Introduction: Positron emission tomography/computed tomography (PET/CT) is currently considered standard of practice for the management of lymphoma with sensitivity and specificity approaching 100%. However, it is expensive, time-consuming and requires exposure to ionizing radiation. Whole body-diffusion weighted imaging (WB-DWI), does not involve exposure to ionizing radiation, is more widely available and can be performed within an acceptable time frame. PET/CT will be used as a reference standard in the evaluation of the value of WB-DWI in the initial staging and treatment response in patients with lymphoma.
Methods: Nine patients with newly diagnosed lymphoma and a pre-treatment PET/CT were prospectively recruited. Patients were analyzed with both imaging modalities before treatment initiation and at four-weeks post-completion of chemotherapy. The presence or absence of nodal and extra-nodal involvement was independently assessed by two radiologists blinded to the PET/CT findings. The PET/CT images were assessed by a single nuclear medicine physician.
Results: Compared to PET/CT, the overall sensitivity, specificity and accuracy of WB-DWI in staging were 62%, 98% and 87% respectively and the overall specificity and accuracy for treatment response were both 99%. Majority of false negative findings were a result of small nodes which showed uptake on PET/CT but were either not identified or did not show restricted diffusion. Further false negative and positive findings were due to reduced spatial resolution and increased motion and susceptibility artefact on magnetic resonance imaging (MRI).
Conclusion: WB-DWI may be a viable alternative to PET/CT in the treatment response of lymphoma. However, in terms of staging, PET/CT probably remains the imaging modality of choice.

KEY WORDS: Diffusion magnetic resonance imaging; Lymphoma; Neoplasm staging; Positron-emission tomography; Whole body imaging.

ABBREVIATIONS: PET: Positron Emission Tomography; CT: Computed Tomography; WB-DWI: Whole body diffusion weighted imaging; MRI: Magnetic Resonance Imaging; FDG: Fluoride-oxyglucose.; DLBCL: Diffuse large B-cell lymphoma; PTCL: Peripheral T-cell lymphoma.

INTRODUCTION

Positron emission tomography/computed tomography (PET/CT) following administration of radiotracer 18F fluorodeoxyglucose (18F-FDG) is currently considered standard of practice for

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the management of lymphoma.[1] The diagnostic sensitivity and specificity of PET/CT in the initial staging of intermediate or high grade non-Hodgkin lymphoma has been found to approach 100%.[2] It provides metabolic information by way of a semi-quantitative index, the standardized uptake value (SUV) which has been shown to be useful for determining disease prognosis and treatment response.[3,4]

However, PET/CT is expensive, time-consuming, requires exposure to ionizing radiation and is not widely available as it involves the use of a cyclotron.[5] In addition, FDG is not entirely cancer-specific; brown fat, muscle tissue and other factors such as infection, inflammation and granulomatous disease can also demonstrate increased FDG uptake. On the other hand, magnetic resonance imaging (MRI) although expensive, does not involve exposure to ionizing radiation, is more widely available and provides excellent soft tissue contrast. In addition, with rapidly progressive MRI techniques such as echo planar imaging and parallel imaging techniques, whole body MRI examinations can be performed within an acceptable time frame.

The evaluation of nodal involvement by CT and conventional MRI are dependent on morphology as determined by the response evaluation criteria in solid tumors (RECIST) and the World Health Organization (WHO).[6,7] However, large nodes may be reactive and small nodes can still harbor foci of disease.

Diffusion weighted imaging (DWI) is a non-invasive technique used for imaging molecular movement or diffusion that is responsive to changes in microstructure of biological tissues. Apparent diffusion coefficient (ADC) is a quantitative index of DWI which can be measured by fitting the MRI signal intensity attained from images with different diffusion-weighting to a monoexponential decay model. It is a relatively simple method and can be attained with as few as two sets of DWI data. DWI with ADC can provide useful physiological and functional information with regards to the characterization of lymph nodes.[8,9] Due to high cellularity and high nuclear-to-cytoplasmic ratio, lymphoma results in reduced extra-and intra-cellular dimensions which leads to high signal intensity on DWI and reduced ADC.

Post-treatment, organizing granulation tissue and fibrotic changes are paucicellular. As a result, DWI should be an effective imaging modality to discriminate between viable lymphoma and treated disease. Several studies in varying cancers have suggested that DWI may potentially be able to discriminate between viable residual tumor and non-neoplastic treatment changes post-therapy.[10-14]

PET/CT will be used as a reference standard in the evaluation of the value of whole body DWI (WB-DWI) in the initial staging and treatment response in patients with lymphoma.

METHODS

Patients

From January 2012 to January 2015, nine patients (6 men and 3 women; mean age, 53 years) with newly diagnosed lymphoma and a pre-treatment PET/CT were prospectively recruited in this single centre study.

The study was approved by the local institutional review board and written informed consent was obtained from all study participants. The study was performed in accordance with the ethical standards laid down in the 1964, declaration of Helsinki and all subsequent revisions. Inclusion criteria were as follows: Age between 21 to 80 years, histological diagnosis of lymphoma, scheduled for first line chemotherapy and nodal or extra nodal disease measuring at least two centimeters in size. Exclusion criteria were 1) General contraindications to MRI (such as ferromagnetic implants, pacemakers and claustrophobia), 2) Pregnant or lactating patients, 3) Non-FDG avid or structurally non-measurable lesions in the pre-treatment PET/CT study.

A detailed medical history and physical examination was obtained for all patients along with standard laboratory tests. Symptoms such as unexplained weight loss, fever and night sweats, co-morbidities, and ECOG (Eastern Cooperative Oncology Group) score were recorded and patients were examined for palpable nodes and presence of hepatosplenomegaly. Seven of the nine patients were diagnosed with diffuse large B-cell lymphoma (DLBCL) and the remaining two had peripheral T-cell lymphoma (PTCL). Ann Arbor staging at time of diagnosis was stage IE in one, II in four and one each in IIE, III, IIIE and IV.

All pre-treatment whole body MRI studies were performed from one to 34 days post PET/CT. All patients received standard first-line chemotherapy after the baseline MRI studies. Five patients received R-CHOP [Rituximab, Cyclophosphamide, Hydroxydaunorucibin (Doxorubicin), Oncovin (Vincristine) and Prednisolone], two received MR-CHOP (Methotrexate, CHOP) and remaining two received CHOPE (CHOP, Etoposide).

Imaging Time-points and Techniques

All patients were followed clinically throughout the study and evaluated with both MRI and PET/CT before treatment initiation and at four weeks after completion of chemotherapy.

MRI was performed using a 1.5-T MR system (Siemens, Aera). Patients were scanned from vertex to mid-thigh using a 20-channel head and neck coil, 32-channel spine coil and two 18-channel body coils. The MRI protocol included axial HASTE TIRM, axial FL2D in and out phase, axial DWI b=50, 800, coronal T1 and coronal TIRM. All MR images were reviewed on a picture archiving and communication system (PACS) workstation.

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For PET/CT, patients were scanned from vertex to mid-thigh with an integrated PET/CT that was acquired approximately 60 mins after intravenous injection of a weight-related dose of 18F-FDG tracer under fasting conditions (6 hours). All PET/CT data was evaluated on a computer display in three orthogonal planes (axial, coronal and sagittal).

Image Interpretation

The presence or absence of nodal involvement in each of twenty regions (Table 1) was independently reviewed by two radiologists blinded to the PET/CT results. Any initial disagreements between the two observers about the imaging findings were resolved in consensus. The PET/CT images were reviewed by a single nuclear medicine physician. The presence or absence of extra nodal involvement was also made in the following sites: Lung, liver, spleen, bone marrow, stomach/other gastrointestinal sites, kidneys and others. A total of 27 regions were assessed for each patient with each imaging modality.

All DWI images were qualitatively interpreted in association with ADC maps; hyperintensity on DWI with a corresponding ADC signal which was hypointense to muscle indicated restricted diffusion. For PET/CT, nodal and extra nodal involvement was diagnosed when any area of abnormal focal increase in tracer uptake was visually evident. For quantitative evaluation of WB-DWI, the mean ADC value of the largest involved node in a region was measured directly on ADC maps; the region of interest (ROI) was manually drawn avoiding any areas of necrosis. The SUV of the largest involved node in a region was recorded for PET/CT.

During assessment of both imaging modalities post-completion of chemotherapy, an evaluation of response to treatment was made and categorized into progressive disease, stable disease, partial response and complete response in comparison to the pre-treatment study. New and/or larger foci of disease involvement was interpreted as progressive disease, no significant change in size and distribution of disease was regarded as stable disease, decrease in size and/or number of lesions was interpreted as partial response and no abnormal lesions in the follow-up study was deemed complete response.

Statistical Analysis

Sensitivity, specificity and accuracy of PET/CT and WB-DWI were compared to evaluate the difference between modalities both in the pre-treatment studies and post-completion of chemotherapy. A correlation was also made between SUV and ADC values to determine a possible relationship between the values obtained. This could only be applied to lesions that were found to be positive on both PET/CT and WB-DWI.

Table 1: Twenty Regions of Nodal Involvement that were Independently Assessed by Two Radiologists on WB-DWI and a Single Nuclear Medicine Physician on PET/CT.

No.	Nodal region
1	Waldeyer's ring and retropharyngeal
2	Right cervical/supraclavicular/occipital/pre-auricular
3	Left cervical/supraclavicular/occipital/pre-auricular
4	Right axillary/Pectoral
5	Left axillary/Pectoral
6	Right internal mammary/diaphragmatic
7	Left internal mammary/diaphragmatic
8	Anterior mediastinal
9	Right paratracheal
10	Left paratracheal
11	Subcarinal/posterior Mediastinal
12	Right hilar
13	Left hilar
14	Retroperitoneal (paraaortic/paracaval/inter-aorta-caval/peripancreatic)
15	Abdominal (Periportal/Perisplenic/Periceliac/Perisuperior mesenteric artery/ Periinferior mesenteric artery)
16	Mesenteric
17	Right Iliac
18	Left Iliac
19	Right Inguinal/femoral
20	Left Inguinal/femoral

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RESULTS

Baseline Staging

In the nine patients, PET/CT defined a total of 72 out of 243 (29.6%) regions as positive for disease involvement with 171 out of 243 (70.4%) as being negative.

Compared to PET/CT, the sensitivity and specificity of WB-DWI was 60.3% (38/63) and 100% (116/116) respectively, for nodal disease and 75.0% (6/8) and 92.7% (51/55) respectively for extra-nodal disease. Overall sensitivity, specificity and accuracy of WB-DWI compared to PET/CT was 62.0% (44/71), 97.7% (167/171) and 86.8% (211/243).

In a third (3 out of 9) of the patients, PET/CT was more sensitive in detecting disease in Waldeyer's ring (Figure 1). In two patients, PET/CT was considerably more sensitive with WB-DWI missing 50% (10/20) and 35% (7/20) of nodal regions. This was primarily a result of small nodes which demonstrated uptake on PET/CT but were not identified or did not show restricted diffusion on WB-DWI (Figures 2-5).

One of the patient also exhibited florid pulmonary lesions that were easily seen on PET/CT but did not demonstrate significant signal change on DWI and were misinterpreted as arte fact on ADC (Figure 5). In addition, two extra-nodal regions in the same patient were found to be false positive on WB-DWI, this was due to: 1). Misinterpretation of the spleen as involved as it was hypointense relative to the liver on ADC, PET/CT however, did not reveal increased uptake (Figure 6), 2). Misinterpretation of the stomach as being involved (Figure 7), this was primarily the result of superior spatial resolution of CT compared to MRI as adjacent nodal involvement was misread as gastric involvement on MRI.

WB-DWI was generally effective in the determination of bone marrow infiltration where it was positive on PET/CT (Figure 5). However, there was a false positive result wherein a focus of restricted diffusion was noted in the left posterior ilium

Figure 1: In 3 out of 9 Patients, PET/CT Demonstrated an Asymmetrical Increased Uptake (a,d,g) in Waldeyer's Ring which was Interpreted as Lymphomatous Involvement. However, Corresponding DWI (b,e,h) and ADC (c,f,i) Failed to Show Restricted Diffusion or Asymmetry which may have Led the Readers to Suspect Lymphomatous Involvement.

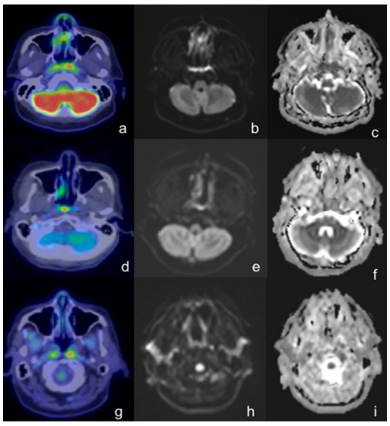

Figure 2: 57-Year-Old Male with Right-Sided Cervical Nodal Involvement was Detected on both Modalities (thin arrow). However, Only Left Cervical Adenopathy was Identified on PET/CT (a, Thick Arrow) with No Evidence of Restricted Diffusion on WB-DWI (b,c).

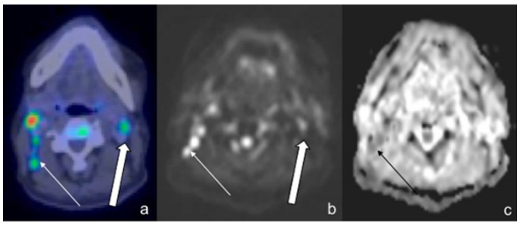

Figure 3: A 57-Year-Old Male with DLBCL. A Small Right Axillary Node with Increased Uptake was detected on PET/CT (a, thin arrow). However, it was not seen on either DWI or ADC images. Note increased uptake on PET/CT in the left upper rib with corresponding restricted diffusion on WB-DWI (b,c, thick arrow)

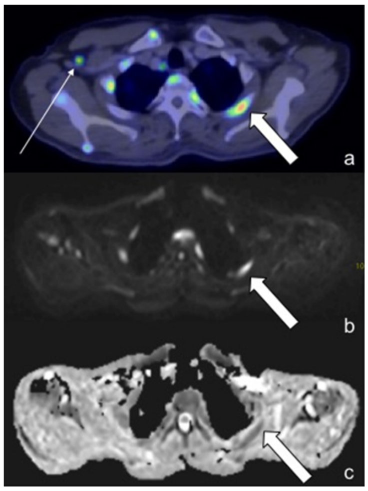

Figure 4: A 65-Year-Old Female with DLBCL. PET/CT Demonstrated Increased Uptake in the Mediastinal Nodes (a, Thin Arrows), However, these were not even Visualized on WB-DWI (b,c). In Contrast, the Right Axillary Node (Thick Arrows) were Positive on both Modalities (a-c).

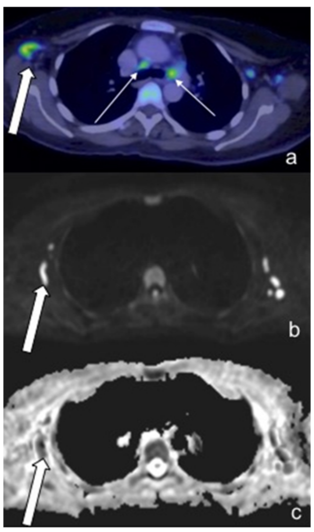

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Figure 5: A 57-Year-Old Male Patient Demonstrated Large Pulmonary Lesions with Intense FDG Uptake (a, Thick Arrow), However, these were Barely Detectable on DWI and Misinterpreted as Artefact on ADC (c, Dashed Arrow). Small Hilar Nodes (a, Thin Arrow) were not seen on WB-DWI. Note Increased FDG Uptake in the Vertebra, Sternum and Ribs with Corresponding Restricted Diffusion.

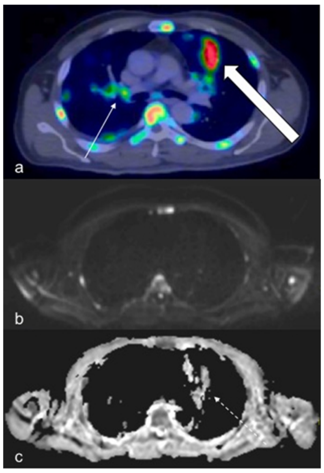


Figure 6: In a 57-Year-Old Male Patient, the Spleen was Misinterpreted as having Lymphomatous Involvement as it was Relatively Hypointense to the Liver on ADC (a, Thin Arrow). However, Findings on PET/CT (b) Demonstrate no Increased Splenic Uptake.

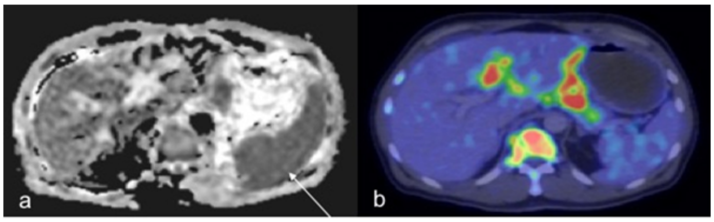


Figure 7: In a 57-Year-Old Male Patient, the Gastric Fundus was Misinterpreted as Being Involved (Thin Arrow) on DWI (a) and ADC (b) as well as on T2W (c) imaging. However, PET/CT was Able to demonstrate a Nodal-focus Separate to that of the Stomach (d, Thick Arrow) illustrating the superior spatial resolution of CT over MRI.

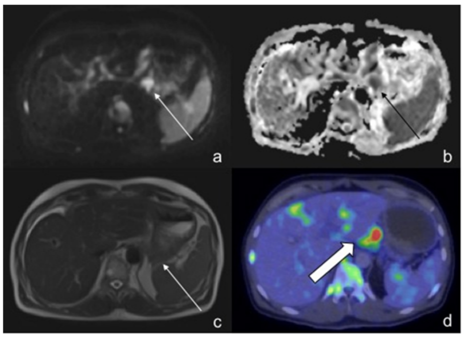
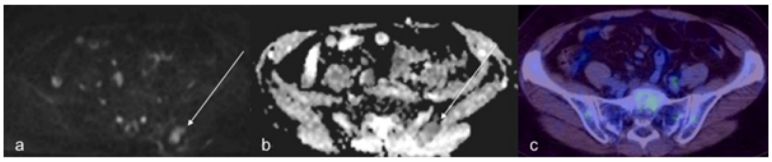


Figure 8: A 65-Year-Old Female Patient with DLBCL, a Focus of Restricted Diffusion (a,b) in the Left Posterior Ilium (thin arrow) was found to be False Positive with no Increased Uptake Detected on PET/CT (c).



that was found to be negative on PET/CT (Figure 8).

Treatment Response

One patient withdrew from the study after the baseline studies. As a result, treatment response could only be assessed for eight patients. All except one patient were assessed as having complete response on PET/CT with the remaining patient deemed as having a partial response with a single extra-nodal region in the caecum demonstrating persistent increased uptake. All except one patient were also assessed as having complete response on WB-DWI with the remaining patient deemed as having a partial response with two false positive nodal regions.

As there was near complete response, true positive findings were not found on WB-DWI compared to PET/CT. Therefore, sensitivity could not be assessed. Compared to PET/CT, the specificity of WB-DWI was 98.8% (158/160) for nodal disease and 100% (55/55) for extra-nodal disease. Overall specificity and accuracy of WB-DWI when compared to PET/CT was 99.1% (213/215) and 98.6% (213/216).

The false negative finding on WB-DWI involved a caecal lesion; it was picked up on pre-treatment WB-DWI as it was distinctively hyperintense whilst the remaining bowel was hypointense. However, on post-treatment images, segments with scattered hyperintensity were also seen in the remaining bowel which made the caecal lesion less conspicuous resulting in it being missed. In contrast, the caecal lesion remained clearly and visually perceptible on PET/CT in both the pre- and post-treatment studies (Figure 9).

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Figure 9: A 65-Year-Old Female Patient with DLBCL, in the Pre-Treatment DWI (a), the Caecal Lesion was Distinctively Hyperintense (Thin Arrow) in Comparison to the Remaining Hypointense Bowel. However, on Post-treatment Studies DWI (d), this was Less Apparent as Other Bowel Loops also Showed Hyperintensity, such as in the Descending Colon (Thick Arrow). ADC Maps (b,e) were not Particularly Useful. In Contrast, the Caecal Lesion was Distinctive in both Pre- and Post-treatment PET/CT Studies (c,f).

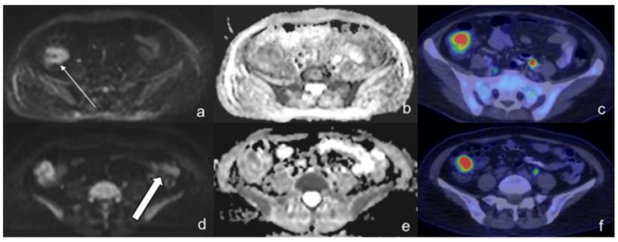
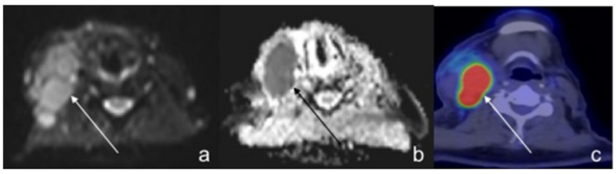


Figure 10: In a 61-Year-Old Male Patient with DLBCL, a Large Right Cervical Node Demonstrated Typical Hyperintensity on DWI (a) with Corresponding Hypointensity on ADC (b) and Intense Uptake on PET/CT (c).



Correlation between SUV and ADC Values

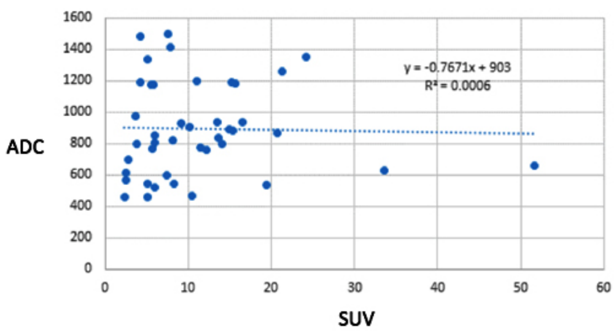
Involved nodes showed increased uptake on PET/CT, high signal intensity on DWI and low signal intensity on ADC maps (Figure 10). The SUV of the largest node in an involved region was compared to the mean ADC value of the largest node in an involved region. There was a total of 43 lesions that were found to be positive both on PET/CT and WB-DWI. One would expect an inverse correlation between the ADC value and the SUV. However, no significant inverse correlation was seen in our study (r=-0.024, p=0.88) (Figure 11).

DISCUSSION

DWI was initially applied in the brain and found to be exceptionally useful for evaluation of restricted diffusion in the diagnosis of acute infarction. However, in recent years, there has been progressively increased use of this technique in the rest of the body.

Lymphomatous tissue, due to increased cellularity and reduced extracellular space results in restricted diffusion (hyperintensity on DWI and hypointensity on ADC). Whole body imaging is desirable in the assessment of hematological malignancies such as lymphoma. Hence, WB-DWI is gaining increased attention as an alternative to PET/CT in the staging and treatment of lymphoma as it can assess the entire body, is radiation-free, more accessible and does not require use of a contrast agent. There are however deficiencies with the use of WB-DWI relative to PET/CT, some of which were illustrated in this study and will be discussed further below.

Figure 11: Plot of ADC against SUV of all Nodal and Extra-Nodal Regions that were found to be Positive on Both PET/CT and WB-DWI. Although an Inverse Correlation was Expected, it was not shown in this Study.



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Waldeyer's ring may exhibit normal high signal on DWI due to relatively low diffusivity and long T2 value.[15] Hence, detection of abnormality in this area on WB-DWI can be difficult as was seen in a third of patients in this study. The asymmetrical increased uptake on PET/CT was not depicted on WB-DWI which may otherwise have led the readers to suspect lymphomatous involvement; this was likely secondary to the high baseline signal on DWI which obscured overlying pathological involvement.

The use of DWI in the chest cavity is limited secondary to artefacts caused by respiratory or cardiac motion. This is likely the cause of the false negative WB-DWI pulmonary findings in one patient where florid lung lesions were depicted on PET/CT. Use of cardiac or respiratory triggering WB-DWI may help to overcome this.[16]

Liver or splenic involvement may be misinterpreted on WB-DWI with the latter occurring in one patient. This may be due to iron content which has been shown to affect DWI visibility and ADC quantification in normal hepatic parenchyma, normal DWI liver visibility is also gender-and age-dependent being superior in women before the age of fifty.[17]

Several artefacts are encountered while assessing the bowel in DWI. Depending on luminal contents, T2-shine through effect will result in hyperintense bowel loops. The true presence of restricted diffusion can then be determined by evaluation of corresponding ADC maps.[18] However, due to inherent heterogeneity of bowel contents, it is frequently challenging to differentiate true restricted diffusion among T2-shine through effect. In addition, bowel peristalsis resulting in motion artefact and inferior spatial resolution of MRI contribute to the challenges in diagnosis of bowel lesions in WB-DWI.

Majority of false negative nodes on WB-MRI were small nodes that were either not even depicted on WB-DWI or did not demonstrate convincing restricted diffusion. This is likely a combination of inherent increased sensitivity of PET imaging which is in the picomolar range[19] and relative increased susceptibility to motion artefact on MRI.[20]

A further shortcoming of WB-DWI is in the assessment of bone marrow. This is particularly important during skeletal maturation. During maturation, hematopoietic marrow is gradually converted to fatty marrow. On DWI, fatty marrow is hypointense secondary to fat suppression whereas red marrow is hyperintense due to relatively higher cellularity. Hence, residual or reactivated islands of red marrow, may conceivably be misinterpreted as lymphomatous involvement in WB-DWI.[15] In contrast, Albano et al[21] conducted a study comparing whole-body MRI, FDG-PET/CT and bone marrow biopsy and found that both MRI and PET/CT were valuable tools for the assessment of bone marrow involvement.

Our results for baseline staging demonstrate that the nodal sensitivity and specificity of WB-DWI compared to PET/CT was 60% and 100% respectively and extra-nodal sensitivity and specificity was 75% and 93% respectively. Overall, WB-DWI showed 62% sensitivity and 98% specificity as compared to PET/CT. Results for treatment response were superior with 99-100% specificity and accuracy for nodal and extra-nodal disease. Compared to PET/CT, the reported sensitivity and specificity for assessment of lymphoma with WB-DWI is 89-100% and 97-100% respectively.[20,22-24] Our results for specificity of WB-DWI are comparable to that of PET/CT (93-100%) and are in line with previous observations. In contrast, our results for sensitivity were inferior to that seen in previous studies; this may be secondary to our small sample size. However, the reduced sensitivity of WB-DWI compared to PET/CT is likely due to inherent increased sensitivity of PET over MRI with many of our false negative results due to small nodes. They demonstrated uptake on PET/CT but were either not seen on or did not show restricted diffusion on WB-DWI.

Our finding of inferiority of WB-MRI in comparison to PET/CT in staging assessment contrasts with several studies[16,24-27] that support DWI as an alternative imaging modality for the initial staging of lymphoma. Although our sample size is small, important differences have been illustrated between the imaging modalities that demonstrate the strength of PET/CT over WB-DWI which account for superiority of PET/CT in baseline staging of lymphoma. This is supported in part by a study conducted by Mayerhoefer et al[20] that found that DWI was slightly inferior to PET/CT with regards to pre-therapeutic regional assessment and staging in patients with FDG-avid lymphoma. However, they found that this was not the case in patients with lymphoma subtypes that showed variable FDG avidity. Another study[22] found that in a minority of their patients with newly diagnosed lymphoma, whole-body DWI led to clinically important over-staging relative to the results of PET/CT thereby concluding that PET/CT remain the reference standard for lymphoma staging lending support to our conclusion.

There were several limitations to this study, the first is having a small number of patients. Despite this drawback, important false positive and false negative findings with respect to WB-DWI were illustrated. We did not perform cardiac or respiratory triggering for WB-DWI resulting in motion artefact limiting evaluation of the mediastinum, lung and left hepatic lobe.[28] The mean ADC value and SUV may have been derived from different nodes within an involved nodal region on WB-DWI and PET/CT respectively; this might have contributed to the poor inverse correlation seen in this study. Lastly, although PET/CT is currently considered the standard of practice in management of lymphoma, using it as a reference standard obscures possible inherent limitations of this modality.

CONCLUSION

In conclusion, WB-DWI may be a viable alternative to PET/CT in the treatment response of lymphoma, this is of particular importance in younger patients to lower radiation burden and future risk of radiation-induced malignancies. In terms of staging however, PET/CT is probably still the superior modality, but if MRI is used instead, care should be taken to understand the limitations of this modality such that has been illustrated above.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

1. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: The Lugano classification. *J Clin Oncol*. 2014; 32(27): 3059-3068. doi: 10.1200/jco.2013.54.8800

2. la Fougere C, Hundt W, Brockel N, et al. Value of PET/CT versus PET and CT performed as separate investigations in patients with Hodgkin's disease and non-Hodgkin's lymphoma. *Eur J Nucl Med Mol Imaging*. 2006; 33(12): 1417-1425. doi: 10.1007/s00259-006-0171-x

3. Lin C, Itti E, Haioun C, et al. Early 18F-FDG PET for prediction of prognosis in patients with diffuse large B-cell lymphoma: SUV-based assessment versus visual analysis. *J Nucl Med*. 2007; 48(10): 1626-1632. Web site. http://jnm.snmjournals.org/content/48/10/1626.long. Accessed February 18, 2017.

4. Hutchings M, Loft A, Hansen M, et al. FDG-PET after two cycles of chemotherapy predicts treatment failure and progression-free survival in Hodgkin lymphoma. *Blood*. 2006; 107(1): 52-59. doi: 10.1182/blood-2005-06-2252

5. Wu X, Kellokumpu-Lehtinen PL, Pertovaara H, et al. Diffusion-weighted MRI in early chemotherapy response evaluation of patients with diffuse large B-cell lymphoma-a pilot study: Comparison with 2-deoxy-2-fluoro- D-glucose-positron emission tomography/computed tomography. *NMR Biomed*. 2011; 24(10): 1181-1190. doi: 10.1002/nbm.1689

6. Therasse P, Arbuck SG, Eisenhauer EA, et al. New guidelines to evaluate the response to treatment in solid tumors. European organization for research and treatment of cancer, national cancer institute of the united states, national cancer institute of canada. *J Natl Cancer Inst*. 2000; 92(3): 205-216. doi: 10.1093/jnci/92.3.205

7. Miller AB, Hoogstraten B, Staquet M, Winkler A. Reporting results of cancer treatment. *Cancer*. 1981; 47(1): 207-214. doi: 10.1002/1097-0142(19810101)47:1<207::AID-CNCR2820470134>3.0.CO;2-6

8. Sumi M, Ichikawa Y, Nakamura T. Diagnostic ability of apparent diffusion coefficients for lymphomas and carcinomas in the pharynx. *Eur Radiol*. 2007; 17(10): 2631-2637. doi: 10.1007/s00330-007-0588-z

9. Perrone A, Guerrisi P, Izzo L, et al. Diffusion-weighted MRI in cervical lymph nodes: Differentiation between benign and malignant lesions. *Eur J Radiol*. 2011; 77(2): 281-286. doi: 10.1016/j.ejrad.2009.07.039

10. Wieduwilt MJ, Valles F, Issa S, et al. Immunochemotherapy with intensive consolidation for primary CNS lymphoma: A pilot study and prognostic assessment by diffusion-weighted MRI. *Clin Cancer Res*. 2012; 18(4): 1146-1155. doi: 10.1158/1078-0432.CCR-11-0625

11. Wang HJ, Pui MH, Guo Y, Yang D, Pan BT, Zhou XH. Diffusion-weighted MRI in bladder carcinoma: The differentiation between tumor recurrence and benign changes after resection. *Abdom Imaging*. 2014; 39(1): 135-141. doi: 10.1007/s00261-013-0038-0

12. Nural MS, Danaci M, Soyucok A, Okumus NO. Efficiency of apparent diffusion coefficients in differentiation of colorectal tumor recurrences and post-therapeutical soft-tissue changes. *Eur J Radiol*. 2013; 82(10): 1702-1709. doi: 10.1016/j.ejrad.2013.05.025

13. Kim S, Loevner L, Quon H, et al. Diffusion-weighted magnetic resonance imaging for predicting and detecting early response to chemoradiation therapy of squamous cell carcinomas of the head and neck. *Clin Cancer Res*. 2009; 15(3): 986-994. doi: 10.1158/1078-0432.CCR-08-1287

14. Fujimoto H, Kazama T, Nagashima T, et al. Diffusion-weighted imaging reflects pathological therapeutic response and relapse in breast cancer. *Breast Cancer*. 2014; 21(6): 724-731. doi: 10.1007/s12282-013-0449-3

15. Kwee TC, Takahara T, Vermoolen MA, Bierings MB, Mali WP, Nievelstein RA. Whole-body diffusion-weighted imaging for staging malignant lymphoma in children. *Pediatr Radiol*. 2010; 40(10): 1592-602. doi: 10.1007/s00247-010-1775-7

16. Fischer MA, Nanz D, Hany T, et al. Diagnostic accuracy of whole-body MRI/DWI image fusion for detection of malignant tumours: A comparison with PET/CT. *Eur Radiol*. 2011; 21: 246-255. doi: 10.1007/s00330-010-1929-x

ISSN 2473-0947
http://dx.doi.org/10.17140/ROJ-2-114

17. Metens T, Ferraresi KF, Farchione A, Moreno C, Bali MA, Matos C. Normal hepatic parenchyma visibility and ADC quantification on diffusion-weighted MRI at 3 T: Influence of age, gender, and iron content. *Eur Radiol*. 2014; 24(12): 3123-3133. doi: 10.1007/s00330-014-3353-0

18. Dohan A, Taylor S, Hoeffel C, et al. Diffusion-weighted MRI in Crohn's disease: Current status and recommendations. *J Magn Reson Imaging*. 2016; 44(6): 1381-1396. doi: 10.1002/jmri.25325

19. Cavalcanti Filho JL, de Souza Leao Lima R, de Souza Machado Neto L, Kayat Bittencourt L, Domingues RC, da Fonseca LM. PET/CT and vascular disease: Current concepts. *Eur J Radiol*. 2011; 80: 60-67. doi: 10.1016/j.ejrad.2010.12.102

20. Mayerhoefer ME, Karanikas G, Kletter K, et al. Evaluation of diffusion-weighted MRI for pretherapeutic assessment and staging of lymphoma: Results of a prospective study in 140 patients. *Clin Cancer Res*. 2014; 20(11): 2984-2993. doi: 10.1158/1078-0432.CCR-13-3355

21. Albano D, Patti C, Lagalla R, Midiri M, Galia M. Whole-body MRI, FDG-PET/CT, and bone marrow biopsy, for the assessment of bone marrow involvement in patients with newly diagnosed lymphoma. *J Magn Reson Imaging*. 2017; 45(4): 1082-1089. doi: 10.1002/jmri.25439

22. van Ufford HM, Kwee TC, Beek FJ, et al. Newly diagnosed lymphoma: Initial results with whole-body T1-weighted, STIR, and diffusion-weighted MRI compared with 18F-FDG PET/CT. *AJR Am J Roentgenol*. 2011; 196: 662-669. doi: 10.2214/AJR.10.4743

23. Stephane V, Samuel B, Vincent D, et al. Comparison of PET-CT and magnetic resonance diffusion weighted imaging with body suppression (DWIBS) for initial staging of malignant lymphomas. *Eur J Radiol*. 2013; 82(11): 2011-2017. doi: 10.1016/j.ejrad.2013.05.042

24. Gu J, Chan T, Zhang J, Leung AY, Kwong YL, Khong PL. Whole-body diffusion-weighted imaging: The added value to whole-body MRI at initial diagnosis of lymphoma. AJR *Am J Roentgenol*. 2011; 197(3): W384-W391. doi: 10.2214/AJR.10.5692

25. Abdulqadhr G, Molin D, Astrom G, et al. Whole-body diffusion-weighted imaging compared with FDG-PET/CT in staging of lymphoma patients. *Acta Radiol*. 2011; 52(2): 173-180. doi: 10.1258/ar.2010.100246

26. Balbo-Mussetto A, Cirillo S, Bruna R, et al. Whole-body MRI with diffusion-weighted imaging: A valuable alternative to contrast-enhanced CT for initial staging of aggressive lymphoma. *Clin Radiol*. 2016; 71(3): 271-279. doi: 10.1016/j.crad.2015.11.018

27. Chen Y, Zhong J, Wu H, Chen N. The clinical application of whole-body diffusion-weighted imaging in the early assessment of chemotherapeutic effects in lymphoma: The initial experience. *Magn Reson Imaging*. 2012; 30(2): 165-170. doi: 10.1016/j.mri.2011.09.019

28. Naganawa S, Kawai H, Fukatsu H, et al. Diffusion-weighted imaging of the liver: Technical challenges and prospects for the future. *Magn Reson Med Sci*. 2005; 4(4): 175-186.