

A Prospective Study: Investigating the use of oncologist-read CT scans in the investigation of suspected malignant spinal cord compression.

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## DECLARATION

I, Dr Sarah Fairhead, declare that the work on this study is originally my work except where acknowledgements are indicated. This is an unsponsored study and was carried out for educational purposes only as an MMED for a postgraduate degree. I therefore declare no conflict of interest whatsoever.

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## Literature Review

### Definition of Spinal Cord Compression

A 2011 article in the BMJ 'Metastatic spinal cord compression' defined spinal cord compression as "an epidural metastatic lesion causing true displacement of the spinal cord from its normal position in the spinal canal."<sup>(1)</sup> Up to Date states: "we and others consider any radiological evidence of indentation of the thecal sac to be evidence of epidural spinal cord compression".<sup>(2)</sup> A 2005 article in the JCO defined SCC as "compression of the dural sac and its contents by an extradural mass."<sup>(7)</sup> On further review of the literature, it is apparent that there is a spectrum of criteria used to define spinal cord compression, ranging from epidural cancer without visible compression to spinal cord displacement. One retrospective cohort study found that depending on the definition used, the percentage of suspected SCC patients diagnosed with this condition varied from 8% to 36%.<sup>(3)</sup>

### Epidemiology

Spinal cord compression (SCC) is a common complication of stage IV cancer, occurring in 2-5% of patients who die from their cancer.<sup>(4,5)</sup> The incidence of this condition varies depending on the primary site of the cancer, with one registry reporting an incidence of 0.2% for pancreatic cancer compared to that of 7.9% in myeloma<sup>(6)</sup>. Amongst the most common primary tumours are myeloma, renal cell carcinoma, prostate cancer and breast cancer. Patients with these primaries also frequently have more than one episode of spinal cord compression.<sup>(1)</sup>

### Anatomy and Pathophysiology

The spinal cord exists within the vertebral canal and in adults extends from the foramen magnum to the T12-L3 vertebral level. Below this level lies the cauda equina which consists of the second to the fifth lumbar and the first to the fifth sacral nerve roots lying in cerebrospinal fluid. The spinal cord itself is surrounded by the thecal sac which is made up of a layer of dura mater containing cerebrospinal fluid. The thecal sac is then surrounded by the epidural space which contains the epidural venous plexus. These structures are surrounded by the vertebral bones. At each vertebral level, paired sensory and motor nerve roots exit the spinal cord.

Most cases of spinal cord compression are due to metastatic spread of tumour to the vertebral bodies. Weakening of the vertebral bodies can result in collapse of these bones into the thecal sac. Primary and secondary tumours as well as nodal masses can also directly invade through the neural foramen into the epidural space. The consequence of this is obstruction of the venous plexus and increased permeability of the veins. This results in oedema, compression of the small arterioles which supply the cord, and finally ischaemia, then infarction of the spinal cord.<sup>(6)</sup>

### Symptoms

Pain is usually the first symptom of spinal cord compression. This pain can be localised to the area of compression or can be radicular in nature. Weakness follows

the pain in the majority of patients. Studies have shown that up to 50 percent of patients have neurological fallout to the degree that they are unable to walk at the time of diagnosis.<sup>(7,8)</sup> Sphincter dysfunction (bladder and / or bowel) is a late finding in spinal cord compression.<sup>(7,8)</sup>

## Management

The management of patients with suspected SCC begins with symptomatic treatment. Patients frequently require opioid analgesia to be examined and to undergo the necessary imaging investigations. The administration of high dose glucocorticoids should also be immediate as this has been shown to improve outcomes in these patients as well as to assist with symptom control.<sup>(9)</sup>

When the diagnosis of SCC has been confirmed, treatment options include surgical resection followed by external beam radiotherapy, external beam radiotherapy alone, and systemic therapy (for chemotherapy sensitive histologies). The choice of treatment depends on the performance status and life expectancy of the patient, the extent of disease and stability of the spine, the radiosensitivity of the tumour, and the resources available at the treating institution. Surgical management is preferred for patients with a good performance status, longer life expectancy, and a single level of cord compression.<sup>(10)</sup> Patients who do not fulfil these criteria are better candidates for radiotherapy.

Standard radiotherapy covers the area of compression as assessed on MRI, along with one vertebra above and one vertebra below this area, and a 1 cm margin circumferentially. If the patient has had surgery, any hardware used should also be treated with a margin. If CT or plain film imaging were used instead of MRI, two vertebrae above and two below should be included.<sup>(11)</sup>

## Prognosis

Spinal cord compression is a poor prognostic factor for malignancy, with median survivals following diagnosis of approximately three months.<sup>(3)</sup> Patients with good prognostic factors, such as slow progression of symptoms and lack of other bone metastases have up to six month survival rates of up to 80%. Those with poor prognostic factors have expected six month survival rates of approximately 14 %.<sup>(12)</sup>

Studies have shown that delays between symptom onset and treatment significantly worsens neurological outcomes.<sup>(13)</sup> Patients who are ambulatory before treatment seem to have better ambulatory rates (in some series up to 100%<sup>(14)</sup>) after treatment. Ambulatory status post radiotherapy has also been linked to improved survival outcomes. One study reported that ambulatory patients had a mean overall survival of 7.9 months whereas non-ambulatory patients had a mean overall survival of 1.2 months. Treating spinal cord compression is thus considered an oncological emergency.<sup>(13)</sup>

## History of Diagnostic Modalities

Historically, contrast myelograms, computed tomography (CT) scans and most recently magnetic resonance imaging (MRI) scans have been used to diagnose spinal cord compression.

Early myelography involved a lumbar puncture with the injection of contrast into the spinal canal followed by fluoroscopy. This modality carries significant risks due to its invasive nature and is contraindicated in patients with brain metastases, thrombocytopenia and coagulopathies.<sup>(2)</sup> There are also risks associated with the use of contrast as well as exposure to ionising radiation.<sup>(12)</sup> However, because of its high sensitivity and specificity, myelography was the early gold standard investigation for spinal cord compression.

CT scan technology was first invented in 1972 but only became readily available in the early 1980's. These scans combine a series of x-ray images with tomographic rotational slices. When the images produced are reconstructed using computer software, they create a series of cross sectional images which can be then be viewed in multiple planes.<sup>(15)</sup>

A small retrospective analysis by Wang et al (1984)<sup>(16)</sup> described the diagnostic capabilities of CT scan in assessing spinal cord compression. CT scans for fifty patients who had presented with possible spinal cord compression were reviewed. It was found that in 48 (96%) of these cases, CT scan was sufficient to diagnose SCC. In two cases, CT was inadequate and myelography was required for this indication. In eight of the 48 cases, myelography was performed in addition to CT (for reasons not specified) and the findings were concordant. In the remaining 42 cases, only CT scan was performed. A major shortcoming of this study, therefore, was that in 84% of cases, CT scan was assessed to be adequate without a gold standard investigation performed to confirm the diagnosis.<sup>(16)</sup>

An analysis of outcomes for SCC published in 1999 provided data suggesting that spinal CT is a safe modality to use in suspected SCC. This retrospective study, evaluated the results of a 90 day follow-up in patients with SCC in an era when SCC was assessed using CT scan. The results of this analysis showed that the majority of patients whose CT scans were negative for SCC did not have new symptoms of SCC or further positive findings on imaging studies in the 90 day followup.<sup>(3)</sup>

Dr DiChiro and Schellinger first published their experience combining CT with myelography in 1976. This combination, although labour and resource intensive, was found to often work better than either alone.<sup>(17)</sup>

CT scan, myelography and CT myelography were commonly used for evaluating spinal cord compression in the 1980's and 1990's.

The first MRI scan was performed on a live patient on July 3, 1977. Six years later, the first commercial MRI scan was launched in Japan. In the years which followed, this modality became increasingly readily available.<sup>(18)</sup> MRI scanners use

strong magnetic fields along with radiowaves and sophisticated software to distinguish between various types of tissue in the body and produce high quality and detailed images.<sup>(19)</sup>

MRI was seen to excel in its ability to visualise soft tissue structures of the spinal cord and soon after the introduction of this investigation, myelography and CT scan fell out of favour in assessing spinal cord compression.

A few small retrospective analyses compared the diagnostic abilities of MRI and myelography in the late 1980's when MRI was becoming more available and reported sensitivities and specificities for MRI ranging from 44-83% and 96-98% respectively. <sup>(7, 20, 21)</sup> One review at the Royal Marsden Hospital found that MRI was equivalent to or better than myelography when assessing for spinal cord compression in 18 of 21 (85.7%) patients and inferior in 3 of 21 (14.3%) patients. The reported findings of this study were that "MRI is the method of choice for the investigation of patients with suspected metastatic spinal cord compression."<sup>(22)</sup>

Another study performed at the Department of Radiology in Ohio compared MRI with CT with or without myelography in assessing tumours of the spine. Twelve patients were reviewed assessing five radiological parameters per patient. There were thus sixty points analysed. It was found that CT and MRI were equivalent in assessing fifty-four points. In three of the remaining points MRI was superior because of its spinal canal imaging capabilities. In these three, CT myelograms were then performed. Of note, differences were found comparing CT myelography to MRI when evaluating the spinal canal.<sup>(23)</sup>

A 2011 study was performed to assess the use of CT scans to triage patients with suspected SCC and produced encouraging results. Radiology registrars at an institution in the UK were asked to assess CT scans of patients with suspected SCC and determine if neural compression was present on the scans. The responses were then compared with the reported results of the diagnostic MRI scans that all patients subsequently had. This research aimed to assess the use of radiologist- reviewed whole spine CT scans for triaging patients with suspected SCC.

The study reported radiologist-reviewed CT to have a high sensitivity (88.9%) and specificity (92%) in detecting metastatic spinal cord compression. The accuracy of CT to assess the level of compression was not assessed in this study.<sup>(24)</sup>

There are no large published studies assessing the use of modern CT scan or oncologist- reviewed CT scan to guide the diagnosis and management of SCC.

### CT Scan Benefits and Risks

CT scans provide images with resolution far superior to plain films. Their ability to demonstrate bone destruction, mineralization and remodelling exceeds that of MRI, whereas MRI is superior in providing information regarding soft tissue structures including the dural sac and spinal cord.<sup>(25)</sup>

CT scans are non-invasive, relatively fast investigations. Benefits of CT scan include a shorter acquisition time which make this investigation more time efficient and less sensitive to patient motion. CT scans are thus easier to perform in patients who are claustrophobic. Unlike MRI, CT scan can be performed at no risk to patients with implantable medical devices.<sup>(25)</sup>

There is much controversy surrounding the carcinogenic risk of CT imaging. The dose of radiation received from a diagnostic CT scan is approximately 1 to 10 mSv. As no prospective trials could ever be done to assess the risk of radiation induced cancers, data from survivors of the atomic bombs have been used to estimate the carcinogenic risk of radiation. The dose from a single CT scan is slightly less than the lowest doses received by some of the survivors of the Hiroshima atomic bombs. These survivors have been closely studied and appear to have a slightly increased risk of cancer mortality compared to the normal population. One CT scan has been said to increase relative cancer related mortality risk by 0.005%.<sup>(26)</sup>

CT scans frequently use iodine contrast, which is known to be nephrotoxic and cause allergic reactions.

### MRI Scan Benefits and Risks

MRI is considered the gold standard in investigating spinal cord compression because of its excellent soft tissue visualisation. This modality uses radiofrequency radiation which is similar to normal background radiation and therefore poses no carcinogenic risk. The contrast used in MRI scans is gadolinium, which is less nephrotoxic and does not typically cause allergic reactions.

The acquisition time for a full spine MRI depends on the sequences performed and the machine used. This time can be between 30 and 60 minutes.<sup>(27)</sup>

MRI scans are substantially more costly than CT scans and as a result, less readily available in resource-constrained settings.

MRI scanners use magnets which may interfere with the functioning of metal containing cardiac pacemakers and valves. Metal prosthetic joints can interfere with the quality of MRI image.<sup>(25)</sup>

### Current Guidelines

Current guidelines support the use of whole spine MRIs for patients with suspected metastatic spinal cord compression.<sup>(28)</sup> It is recommended that initial sequences include sagittal T1 and/or STIR to diagnose the presence of spinal metastases. Following this, T2 images determine if compression is present and further characterise any compression. Studies have found that patients frequently have multiple levels of compression which may be missed if only the region which is clinically suspected to be compressed is imaged. For this reason, it is recommended that the whole spine is imaged.<sup>(6)</sup> The use of myelography is only advocated if other modalities are contraindicated. CT scan is currently only recommended as an adjunct to MRI in this setting.<sup>(6)</sup>

These guidelines are based on studies which were performed in an era with early CT technology. Modern CT scanners have advanced in a number of ways. Of note is improved soft tissue imaging capabilities, as well as modern reconstruction software which allows the user to assess the images obtained in sagittal, axial and coronal planes. Additionally, high resolution PACS monitors permit magnification and viewing of images with settings specific to the type of tissue being assessed. <sup>(29)</sup>

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## Abstract

Background: Spinal cord compression is a common complication of advanced cancer with significant consequences for individual patients and health care systems as a whole. This condition requires a radiologist reported MRI scan to diagnose, which is a limited resource in many settings. There are no data comparing MRI with multi-detector CT scan, a more accessible resource, for the diagnosis of this condition.

Objectives: To investigate whether CT scans assessed by radiation oncologists should be used to diagnose and manage spinal cord compression in patients with advanced cancer by assessing its overall accuracy, including sensitivity and specificity, as a diagnostic test. To collect preliminary data to assist in ethically sound decision making regarding the rational allocation of MRI scans, which are known to be a scarce medical resource.

Methods: Eight radiation oncologists (RO's) were given case histories and CT scan images for twenty cancer patients who had presented with possible spinal cord compression (SCC). They were asked to answer questions aimed to assess whether CT scan can be used to diagnose and guide treatment for spinal cord compression and how accurate an investigation CT scan is in this setting compared to the gold standard, MRI.

Results: In 84% of assessments, RO's were able to correctly identify the absence or presence of SCC using CT scan. In 38% of assessments, RO's were able to correctly identify the level of SCC and would have treated that level exclusively. In 69% of assessments, the correct level would have been treated with or without additional non-compressed levels. The overall accuracy of CT scan to detect the absence or presence of SCC was 84%. The overall sensitivity was 83%. The overall specificity was 85%. Individual RO's scored an average of 83% (range 62-100%) for questions testing their ability to diagnose the absence or presence of SCC using a CT scan. Individual RO's scored an average of 69% (range 38-89%) for questions testing their ability to treat the level of compression and an average of 38% (range 13-56%) for questions testing their ability to treat the level exclusively. In 40% of assessments RO's reported that they would feel confident treating with only a CT scan. Individual RO confidence levels ranged from 0-66%. In 51% of assessments, the RO's would have changed their treatment plans if an MRI reported by a radiologist was available.

Conclusion: Spinal CT scans reported by radiation oncologists are reasonably sensitive and specific for the detection of spinal cord compression. However, this imaging modality should not be used, in centers where radiology reported MRI is available, to diagnose and treat spinal cord compression, due to the relative inaccuracy of this test in determining the appropriate treatment for this condition.

# Article

## Introduction:

Spinal cord compression (SCC) is a common complication of advanced cancer, with approximately 2.5% of cancer patients having spinal cord or cauda equina compression in their final years of life.<sup>(1)</sup> Time is of the essence in the treatment of SCC and delays are associated with poorer outcomes. Late diagnosis of SCC can lead to irreversible neurological deficits, including paralysis and incontinence. The negative impact on quality of life for patients, as well as the additional burden placed on health care systems is significant. The standard of care investigation in diagnosing spinal cord compression is the MRI scan. However, in resource-constrained environments, MRI equipment, staffing and expertise may be inadequate or absent at the point of care. Thus, the waiting time for an MRI may delay treatment and, in some incidences, negatively affect outcome. CT scanners are a more readily available diagnostic modality. This study aimed to assess whether oncologist-read CT scans provide the information required to diagnose and manage metastatic spinal cord compression.

## Background

### Definition and Diagnosis of Spinal Cord Compression

A 2011 article in the BMJ 'Metastatic spinal cord compression' defined spinal cord compression as "an epidural metastatic lesion causing true displacement of the spinal cord from its normal position in the spinal canal."<sup>(2)</sup> Up to Date states: "we and others consider any radiological evidence of indentation of the thecal sac to be evidence of epidural spinal cord compression."<sup>(3)</sup> A 2005 article in the JCO defined SCC as "compression of the dural sac and its contents by an extradural mass."<sup>(4)</sup> On further review of the literature, it is apparent that there is a spectrum of criteria used to define spinal cord compression, ranging from epidural cancer without visible compression to spinal cord displacement. One retrospective study found that depending on the definition used, the percentage of suspected SCC patients diagnosed with this condition varied from 8% to 36%.<sup>(4)</sup>

Historically, contrast myelograms, computed tomography (CT) scans and most recently magnetic resonance imaging (MRI) scans have been used to diagnose spinal cord compression.

CT scans combine a series of x-ray images with tomographic rotational slices to produce reconstructed images which can be viewed in multiple planes. This modality was first discovered in 1972 and has been used in clinical practice since the beginning of the 1980's. Contrast myelograms use the injection of a contrast agent into the subarachnoid space followed by fluoroscopy or CT scanning to visualise the contents of the thecal sac. Small studies in the 1980's reported that the correlation between CT and myelography was very good, although myelography was minimally more sensitive and was thus used as the gold standard test.<sup>(5)</sup> CT

myelography, a combination of the two modalities was also sometimes used for the diagnosis of SCC.

MRI scan, which uses magnetic fields and radiowaves to image the body without the use of ionising radiation, became readily available in the 1980's and was found to be superior to myelography in its ability to accurately image the soft tissue within the thecal sac and epidural space<sup>(9)</sup>. Studies comparing myelography and MRI for evaluating possible SCC produced conflicting results, with some showing myelography to be superior and others favouring MRI.<sup>(6,7,8)</sup> Benefits of MRI include its ability to image the bone and soft tissue adjacent to the cord, capabilities in imaging the thecal sac regardless of the presence of spinal subarachnoid block, and its non-invasive nature.<sup>3</sup>

Numerous small studies have compared the usefulness of these modalities in the diagnosis and treatment planning for patients with vertebral bony metastases and primary bone tumours. The general consensus of these studies was that CT scan is superior in its ability to demonstrate calcified tumour matrix and bony detail whereas MRI is superior in providing information regarding the adjacent soft tissues including extent into the spinal canal.<sup>(9,10)</sup>

Consequently MRI has become the preferred modality for imaging the spinal cord. Current guidelines support the use of whole spine MRIs for patients with known malignancy and suspected metastatic spinal cord compression.<sup>(1)</sup> Studies have found that patients frequently have multiple levels of compression which may be missed if only assessing the region which is clinically suspected.<sup>(11)</sup>

Studies comparing CT and MRI capabilities for assessing the vertebral column are all twenty to thirty years old and not reflective of the capabilities of modern CT and MRI scans. In the time since clinicians have started using MRI as the gold standard, vast improvements have been made in CT technology.<sup>(12)</sup> Modern CT scanners have improved soft tissue imaging capabilities as well as reconstruction software to allow visualisation of images in multiple planes. Medical imaging using high resolution PACS monitors allows for magnification and viewing of images with settings specific to the type of tissue being assessed.<sup>(13)</sup> Benefits of CT scan include a shorter acquisition time, making this investigation more time efficient and less sensitive to patient motion. CT scans are also better tolerated for patients who are claustrophobic and unlike MRI's, can be performed at no risk to patients with implantable medical devices.<sup>(14)</sup> As CT scans use ionising radiation, MRI scans are preferred in young patients and patients with longer life expectancies, due to the possible risk of second malignancy.<sup>(15)</sup> Although the majority of patients with metastatic spinal cord compression have a life expectancy of only a few months, certain types of cancers such as testicular seminoma can be stage IV with a much better prognosis. The risk of second malignancy should be considered in these patients when choosing a diagnostic modality.

There have, to our knowledge, been no dedicated studies comparing the use of modern multi-detector CT scan and MRI in detecting and guiding the treatment for spinal cord compression in the setting of known malignancy.

An analysis of outcomes for SCC published in 1999 provided data suggesting that spinal CT is a safe modality to use in suspected SCC. This retrospective study followed up the outcomes of patients with SCC who had been assessed using spinal CT scan. The results of this analysis showed that the majority of patients whose CT scans were negative for SCC did not have new symptoms of SCC or further positive findings on imaging studies in the 90 day followup<sup>(4)</sup>

A more recent study, which assessed the utility of CT scans in triaging patients with possible SCC, reported CT to have a sensitivity of 89% and a specificity of 92% (using MRI as gold standard). This study, however, used radiologists to interpret the CT scans and did not investigate the use of CT for guiding treatment decisions in these cases.<sup>(16)</sup>

### **Management of Spinal Cord Compression**

When the diagnosis of SCC has been confirmed, surgical resection followed by radiotherapy, radiotherapy alone and systemic therapy (for chemotherapy sensitive histologies) are the treatment options. The performance status and prognosis of the patient, extent and focality of compression, assessed stability of the spine, radiosensitivity of the tumour, and available resources are all factors taken into consideration when determining the optimal treatment for this condition.

Approximately 70% of patients report an improvement in their pain score following radiotherapy. If given early enough, this modality may improve neurological function and prevent the progression of symptoms. Patients who are ambulatory at diagnosis generally remain ambulatory after treatment. Approximately 30% of non-ambulatory patients regain ambulation after radiotherapy. This figure is higher in tumours with radiosensitive pathologies such as lymphoma, myeloma, seminoma, and small cell lung cancer.<sup>(17)</sup>

### **The Groote Schuur Experience**

At Groote Schuur Hospital, oncology patients with suspected spinal cord compression are investigated with an MRI scan.

Our institution has one MRI scanner operating routinely between the hours of 8 am and 6 pm with an average weekly throughput of 100 patients. Motivated after hours scanning is available on a call-out basis. Approximately 90% of the scans are elective (non-emergency) cases with a waiting time of three to four months. This leaves approximately ten slots per week for emergency cases. It is estimated that the oncology department uses approximately one third of these slots for patients with suspected spinal cord compression.

Because of the demand for this machine, arranging an urgent MRI scan for a patient with suspected spinal cord compression is a complex time consuming process designed to ensure that this resource is used appropriately. Approved cases are placed on a waiting list with other emergencies for the day. The duration of a limited non-enhanced MRI of the spine is approximately 20-30 minutes. The interpretation of the MRI scan and report may take a further 45 minutes. In total this whole process may take half a day.

Arranging a departmental CT scan in the oncology unit is considerably easier and quicker. Acquisition time for a non-enhanced CT scan is under a minute. After scanning, the source images and computer generated reconstructions are available for review, allowing a decision to be made immediately as to whether radiotherapy is required.

The Groote Schuur Hospital MRI scanner was unavailable for a month at the beginning of 2015. During this period, the protocol for suspected SCC was changed to include a preliminary CT scan, followed by transfer of the patient to another hospital for an MRI only if the CT was unable to diagnose compression. It was felt by the treating doctors that the majority of cases seen whilst MRI's were not available were able to be managed with CT scan alone. Successfully managing patients without MRI stimulated doctors in the radiation oncology department to question whether they could assess CT scans themselves to streamline the diagnostic process.

Diagnostic imaging at our institution is assessed and reported on by the radiology department. Patients who are being considered for either curative or palliative radiation therapy undergo an additional planning CT scan which is performed in the oncology department. The radiation oncologist routinely reviews both sets of images when determining a treatment plan, thus developing reasonable proficiency in assessing malignant disease on CT scan.

## **Rationale**

The GSH Radiation Oncology Department requires approximately three MRI scans for suspected spinal cord compression per week. If these scans could be performed using the Oncology Departments CT scanner, it would free up space for other emergency cases which exclusively require MRI for diagnosis, as well as for other elective cases who currently wait for up to three months for an MRI scan due to the Radiology Departments patient load. If patients with spinal cord compression can be adequately investigated with a CT scan, MRI scans would become more available for conditions that cannot be adequately investigated with CT.

In our center, replacing MRI with CT in the workup of these patients might be faster and would decrease the work-load of the MRI department.

Additionally, patients presenting with suspected spinal cord compression are generally frail, emotionally vulnerable, and often in severe pain which is exacerbated by lying on their backs for prolonged periods.

Using the CT scanner based in the oncology unit instead of relying on MRI may not only save time in the workup and treatment of patients with possible spinal cord compression, but may also significantly reduce patient discomfort during the diagnostic phase of hospitalisation.

## Objectives

1. To assess whether CT scans assessed by radiation oncologists should be used to diagnose and manage spinal cord compression in patients with advanced cancer by assessing its overall accuracy including sensitivity and specificity as a diagnostic test.
2. To collect preliminary data to assist in ethically sound decision making regarding the rational allocation of MRI scans, which are known to be a scarce medical resource

## **Methods**

The study was conducted in the Radiation Oncology Division of Groote Schuur Hospital between the months of August 2015 and February 2016. Patients aged 18 years and over, with proven malignant disease presenting with symptoms and signs of spinal cord compression were eligible to participate. Patients known to have other neurological diseases, brain metastases, those presenting after hours, those who would not benefit from emergency radiotherapy, and those assessed not to be physically or emotionally fit enough to participate in the study were excluded. Following the identification of an eligible participant, the individual was approached by the recruiting doctor and counselled regarding the study in a private environment. Interpreters were used as needed.

All participants (patient and doctors) provided written informed consent and the study was approved by the ethics committee at Groote Schuur (HREC REF:425/2015. June 2015).

Of the 21 patients considered for enrolment, four were excluded from the study as they did not fulfil enrolment criteria; one at the outset and the other three after the questionnaires had been completed, thus leaving 17 patients who were included in the analysis.

The study participants underwent MRI and CT scans of their spines. The MRI scans were done on Siemens Aera 1.5T scanner. A limited protocol was performed which included T2 weighted sagittals as well as axial images through any suspicious regions. The CT scans were done with 5mm thickness, on the GSH Oncology department's Toshiba Aquilion TSX-201A scanner. No contrast was given for MRI or CT.

The MRI scans (reported by radiologists) were used by their treating doctors to assess for and guide the treatment of any spinal cord compression. The non-enhanced CT scans were performed in the radiation oncology department using the CT scanner which is routinely used for planning radiotherapy for the oncology patients.

Eight radiation oncologists, (four consultants and four senior registrars) were selected to assess the CT scan images. Potential participant names were placed in a hat and randomly selected. Patients were divided into two groups. Two registrars and two consultants were assigned to each of the patient groups. A total of 68 assessments were therefore performed. Patients were assessed by answering five questions related to their diagnosis and treatment. The doctors were given a brief history and summary of the clinical findings for each patients to assist them in the answering of these questions. The doctors were blinded to the identity of the patients and non-essential information, such as age and background, were omitted from the histories to prevent bias.

The CT data was transferred to “Dicom Radiant” imaging software. This software, a product of Medixant, is a PACS-DICOM viewer for medical images which allows for zooming and panning, changing window settings for bone and soft tissue, the use of cross reference lines to browse in different image planes, as well as multi-planar reconstruction.

The doctors were given as much time as they needed to go through the images and answer the questions.

The questions asked the doctors to assess whether each patient had spinal cord compression, what vertebral levels the doctors would treat with radiotherapy, and whether they would feel confident treating each patient on the basis of the reviewed CT scan. They were then shown the actual MRI reports for each of the patients and asked whether their treatment plans would differ with this extra information. They were also invited to share any additional comments which they believed may be helpful. The responses were then analysed using the radiologist reported MRI as gold standard.

### Design and Data Analysis

This was a descriptive study that included the collection of both qualitative and quantitative data. The responses from the individual questionnaires were collated and analysed using calculations described below.

#### Question One:

**Would you assess this patient to have spinal cord compression?  
Yes or no?**

The overall accuracy of diagnosis based on a CT scan was calculated for individual scorers as well as for the total number of assessments as follows:

The total percentage of patients who would be accurately diagnosed for SCC:

$$\frac{\Sigma \text{ correct answers (total)}}{\Sigma \text{ assessments (total)}} \times 100$$

The percentage of patients who would be accurately diagnosed for SCC by each individual assessor:

$$\frac{\Sigma \text{ correct answers (individual assessors)}}{\Sigma \text{ assessments (individual assessors)}} \times 100$$

Note: If the reported MRI diagnosed SCC, the correct answer was Yes (SCC present). If SCC was not diagnosed, the correct answer was No (SCC absent).

Sensitivity and specificity were calculated using this data with the following equations:

$$Sen = \frac{TP}{TP+FN} \times 100$$

$$Sp = \frac{TN}{(TN+FP)} \times 100$$

where TP represents true positives, TN represents true negatives, FP represents false positives and FN represents false negatives.

### **Question Two:**

#### **What vertebral levels would you treat with radiotherapy?**

The answers for this question were analysed to determine:

- A. The percentage of assessments where the level of cord or cauda compression would be correctly treated (level included) regardless of whether extra areas were also treated. A percentage was calculated for all of the assessments (total) as well as for each individual assessor (individual assessor).

$$A_i = \frac{\Sigma \text{ level included (total)}}{\Sigma \text{ assessments (total)}} \times 100$$

$$A_i = \frac{\Sigma \text{ level included (individual)}}{\Sigma \text{ assessments (individual)}} \times 100$$

- B. The percentage of assessments where the level of compression would be treated exclusively (level exclusive).

$$B = \frac{\Sigma \text{ level exclusive (total)}}{\Sigma \text{ assessments (total)}} \times 100$$

The level(s) of cord / cauda compression diagnosed on the reported MRI's were used as correct answers for the questions.

False positive and false negative responses from Question One ("Would you assess this patient to have spinal cord compression?") by default scored incorrectly for Question Two.

**Question Three:**

**Would you be able to confidently treat using only the CT scan?  
Yes or No.**

The total percentage of assessments where doctors were confident that the CT scan provided sufficient information to make a treatment plan given the level of suspicion for SCC was calculated with the following equation:

$$\frac{\Sigma \text{ RO's confident}}{\Sigma \text{ assessments (total)}} \times 100$$

Where RO's confident represents assessments where radiation oncologists were confident using a CT scan to diagnose SCC and assessments (total) represents the assessments performed for all of the cases (n=68).

**Question Four:**

**Do you have any additional comments  
which you feel may be helpful?**

The answers for this question were analysed descriptively.

**Question Five:**

**Now view the MRI scan for this patient with the radiology report.  
Would you change your treatment plan?  
Which levels would you now treat?**

The total percentage of assessments where the information provided by an MRI scan would change the treatment plan for a patient was calculated with the following equation

$$\frac{\Sigma \text{ change plan}}{\Sigma \text{ assessments (total)}} \times 100$$

where change plan represents the assessments where radiation oncologists would change their treatment plan with the information provided by an MRI and assessments (total) represents the assessments performed for all of the cases (n=68).

## Results

### Patient Characteristics

Of the seventeen patients included in the study, 47% (n=8) were women and 53% (n=9) were men. The age of these patients ranged between 32 and 78 years with an average age of 58 years. There were a variety of primary diagnoses, with breast (n=4), prostate (n=4) and unknown primary (n=4) being the most common.

Table 1: Patient Characteristics

Characteristic	N (%)
<b>Age</b>	
Mean	58
Range	32 - 78
<b>Gender</b>	
Male	9
Female	8
<b>Tumour site</b>	
Breast	4
Prostate	4
Lymphoma	2
Unknown Primary	3
Lung	2
Renal cell carcinoma	1
Rectal	1
<b>Years since diagnosis</b>	
Mean	2
Range	1 - 11

## Results Based on MRI Scans

Of the seventeen patients included in the study, thirteen patients had SCC diagnosed on MRI, four had no evidence of SCC and one did not have SCC but had evidence of malignant compression of an exiting nerve root. Multiple levels of cord compression were seen in 62% of the cases.

## CT Scan To Guide Diagnosis and Treatment of Spinal Cord Compression

### **Overall Patient Assessment Using CT Scan**

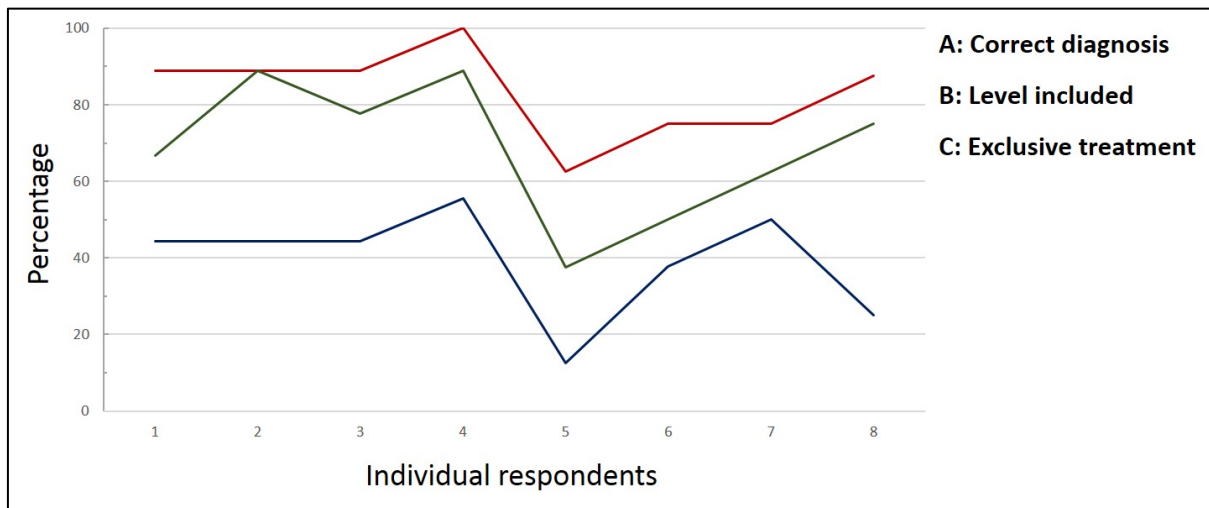
The questionnaires were analysed to assess the accuracy of CT scan to diagnose and treat SCC. In 84% of assessments, the RO's were able to correctly identify the absence or presence of SCC using CT scan.

However, in only 38% of assessments the RO's were able to correctly identify the level of spinal cord compression and would have treated that level exclusively. In 69% of assessments, the correct level would have been treated irrespective of whether additional levels were included.

### *Sensitivity, Specificity and Accuracy of CT Scan To Diagnose Spinal Cord Compression*

The overall accuracy of CT scan to detect the absence or presence of spinal cord compression was 84%. The sensitivity (positive predictive value) was 83%. The specificity (negative predictive value) was 85%.

## Analysis of Results for Individual Radiation Oncologists



**Figure 1.** The Accuracy of Individual Respondents. Graphical Representation of Interscorer Variability In Diagnosis and Precision of Treatment.

Figure 1 compares the individual percentages of correct answers obtained for each RO with respect to **A:** diagnosis of SCC, **B:** treatment of the compressed level regardless of whether additional levels were treated, **C:** exclusive treatment of the compressed level.

Individual RO's scored an average of 83% (range 62-100%) when answering questions testing their ability to diagnose the absence or presence of SCC using CT scan, an average of 69% (range 38-89%) for questions testing their ability to treat the level of compression, and an average of 38% (range 13-56%), for questions testing their ability to treat the level exclusively .

Figure 1 summarised the accuracy of decisions regarding diagnosis and treatment according to the individual scorer. The aggregate information from Figure 1 is shown in Table 2.

Table 2: Range of Accuracy of Respondents

		<=25%	<=50	<=80%	80-95%	95-100%
1	True positive Dx*	0	12.5%	37.5%	12.5%	50%
2	True negative Dx	0	0	37.5%	0	62.5%
3	Total True Dx	0	0	37.5%	50%	12.5%
4	Exclusive Tx**	25%	87.5%	100%	0	0
5	Level Included in Tx	0	25%	75%	25%	0

\*Dx= diagnoses

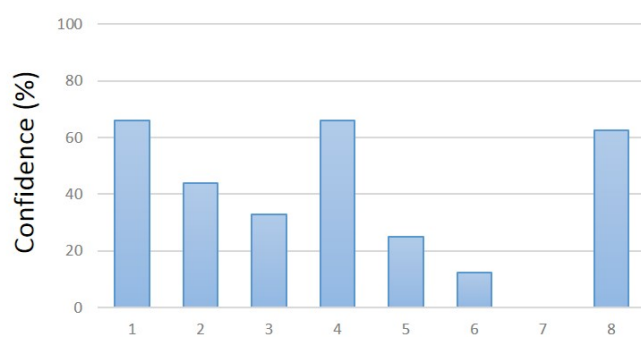
\*\* Tx= treatment

Table 2 depicts the range of accuracy for RO's in identifying and treating SCC using a CT scan by demonstrating the percentage of RO's who correctly diagnosed and treated for each category listed (1-5).

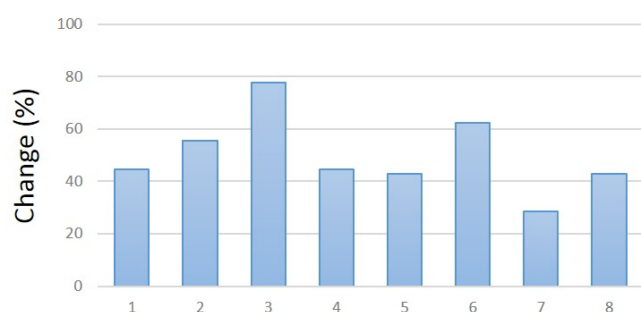
The results revealed that 62.5% of RO's could diagnose the presence of SCC in at least 80% of cases, and only 50% of RO's could diagnose the presence of SCC in more than 90% of cases. The results further reveal that 62.5% of RO's could detect the absence of SCC with 80% accuracy. Overall, 37.5% of RO's scored less than 80% for accuracy in their diagnosis of SCC using the CT scan. (Table 2).

The correct area would be treated in at least 80% of cases by only 25% of RO's. In addition, none of the RO's would give the exact correct treatment in more than 80% of cases. (Table 2).

### *Level of Confidence of Radiation Oncologists Using a CT Scan*



**A.** Individual respondents



**B.** Individual respondents

**Figure 2.** Overall Confidence When Using a CT Scan. **A:** The Percentage of Cases Where Individual Radiation Oncologist Felt Confident Diagnosing and Treating SCC. **B:** The Percentage of Cases Where Treatment Plans Would Be Changed Based on Additional Information From an MRI

In 40% of assessments, the radiation oncologists reported that they would feel confident treating with only a CT scan. However, individual RO's confidence levels ranged from 0-66%.

In 51% of assessments, the RO's would have changed their treatment plans if an MRI reported by a radiologist was available. Individual RO's reported that they would change their treatment plan on average in 50% (26-78%) of assessments.

### **Additional Comments Given By Doctors**

The majority of RO's did not respond to this question.

However, a doctor reported that CT scan was not sufficient in cases with multiple levels of disease as MRI would provide additional detail to guide the order in which to treat the various levels. Two doctors reported that the C-spine was more difficult to assess with CT scan.

The radiologist report was also reported to be especially helpful in cases with foraminal compression.

Consensus was that MRI is quicker and easier to assess than CT.

Overall, CT scan was shown to be accurate in diagnosing the presence or absence of spinal cord compression. However, the accuracy of treatment decisions was low and radiation oncologists reported low levels of confidence when using this diagnostic modality.

### **Discussion**

The public health sector in South Africa is a resource-constrained setting. As such, the rational and fair apportioning of diagnostic investigations is an important consideration. Health care professionals working in this sector face the challenge of making the best use of available resources while at the same time aiming to provide internationally accepted best standard of care. If it can be shown that a less expensive investigation could be used without compromising patient care, then practices may be changed and resources more rationally distributed.

Studies are usually designed to prove that new and frequently more expensive diagnostic technology is better than older technology. However, these new tests are not always readily available to all the patients who need them. Delays in accessing these investigations may lead to worse outcomes.

The gold standard diagnostic investigation for spinal cord compression is the MRI, an expensive, time consuming test which is in high demand for a number of other indications. The objective of this study was to assess whether CT scan could be used

by oncologists to accurately diagnose spinal cord compression in the setting of known malignancy.

Further, it aimed to assess whether CT alone could be used in this setting to accurately plan radiotherapy of the spine. If this was found to be true, resources could be more rationally allocated and the diagnostic workup for patients with spinal cord compression could be streamlined, leading to a better patient experience and acceptable patient outcomes. This would possibly also be of interest to lower income countries where MRI scans are currently not available. If CT scans were found to be an acceptable imaging modality, decision makers would be able to spend their limited budgets on other necessary commodities.

Spinal cord compression due to malignant disease is a serious but potentially treatable condition. If not treated timeously, the consequences are dire with patients left paralysed and frequently incontinent. Quality of life is adversely affected and the additional burden on social support systems is substantial.

Treating patients before they lose ambulation greatly increases their chances of retaining their ability to walk. Those who are non-ambulatory prior to commencing treatment have a better chance of regaining this motor function if they are treated within 12 hours of losing their ability to walk.<sup>(4)</sup> Efficient workup of these patients is therefore crucial. Prior to commencing the study, it was proposed that using CT scan rather than waiting for an MRI may decrease the time taken to workup these patients.

Important considerations tested in this study were the sensitivity and specificity of CT scan in detecting spinal cord compression, the ability of CT scan imaging to show all of the levels of compression and whether treatment plans made by doctors using CT scan included all of the levels requiring treatment.

In the oncology setting, the likelihood of a patient presenting with signs and symptoms of SCC having a positive diagnosis is very high. Using the MRI results as gold standard, over three quarters of the patients in this cohort had a positive diagnosis of spinal cord compression

Previous studies have demonstrated sensitivities of 44-83% and specificities of 96-98% for MRI in diagnosing SCC.<sup>6,18</sup> These values are similar to those found for CT in this study. However, it is important to remember when interpreting the values for CT, that they were calculated with MRI as gold standard, therefore assuming MRI to be 100% accurate.

In 84% of assessments, the radiation oncologists correctly diagnosed the absence or presence of spinal cord compression using CT scan. 62.5% of RO's were able to make the correct diagnosis more than 80% of the time. Furthermore, the sensitivity of radiation oncologist-read CT scans was calculated to be 83%. This means that in 17% of cases, compression would be missed using a CT scan, a high percentage considering the significant consequences for patients and the high pre-test

probability of a positive diagnosis in this patient population. However, of note is that this sensitivity is higher than that reported by previous studies assessing MRI's.

The results for accuracy of treatment utilising CT, however, were less favorable. In this cohort of doctors, only one RO (12.5%) would have given the correct treatment exclusively more than 50% of the time when using a CT scan. The remaining seven doctors (87.5%) would have treated patients incorrectly more than 50% of the time. Six of the doctors (75%) would have geographically missed the correct level up to 20% of the time.

On average, individual doctors would have changed their radiotherapy treatment plan in 50% (range 26-78%) of cases after seeing the MRI with its report . It is interesting to note that this percentage is comparable to the results of previous studies which compared treatment accuracy using MRI versus plain film X-ray and clinical exams.<sup>(11, 18)</sup>

It could be argued that regardless of whether SCC is present, patients presenting with back pain and weakness frequently have vertebral metastases which would benefit from radiotherapy to alleviate their pain and to prevent neurological fall-out from occurring in the future. However, prophylactic radiotherapy may be treatment which would not otherwise have been necessary later. Patients presenting with weakness and no back pain would not require radiotherapy for its analgesic benefit and may not progress to develop cord compression. In such cases, radiotherapy would be considered to be completely unnecessary treatment.

Additionally, if cord compression is assumed based on the presence of vertebral metastases, the true cause of the patients weakness may not be addressed. Cancer patients with metastatic disease may have weakness as a result of paraneoplastic syndromes, brain metastases, leptomeningeal metastases, chemotherapy related neuropathies, cerebrovascular complications of their malignancy, and metabolic disturbances amongst others. Some of these causes such as metabolic disturbances are reversible if identified and treated.

This study found the specificity of oncologist reviewed CT scan to be 85% when used to diagnose spinal cord compression, i.e. 15% of patients are incorrectly diagnosed with SCC when this modality is used. The diagnosis of spinal cord compression is one which carries a large emotional burden for patients. Patients receiving radiotherapy for SCC require hospital admission which means separation from their families. Additionally radiotherapy comes with side effects and risks which may add to the symptom burden of these patients. For CT to replace MRI in this setting, it should therefore be able to not only diagnose the presence of SCC but also to confidently rule out compression when it is absent in order to avoid unneeded treatment. The specificity of this test was thus deemed to be important, and 85% specificity was judged by the authors to be low. Crocker et al reported a specificity of 92% for radiologist reviewed CT scan.<sup>16</sup> The lower specificity may reflect the level of expertise of the doctor rather than the ability of the diagnostic modality.

The doctors participating in this trial frequently commented that vertebral metastases were visible on the CT scans but that cord compression could not definitively be seen. Studies have shown that patients who are treated prophylactically for early asymptomatic SCC may benefit symptomatically from this treatment with minimal side effects.<sup>(20)</sup> To treat patients prophylactically, the imaging modality of choice should show early disease. To use CT scan as an early diagnostic modality one would need to treat malignant vertebral body lesions (easily visible on CT unlike epidural disease) prophylactically with the assumption that these lesions are likely to lead to SCC if untreated. The literature suggests however that only a small percentage (approximately 20%) of patients with bony metastases in the vertebral column progress to develop cord compression.<sup>(21)</sup> Treating bony metastases prophylactically may therefore not be a reasonable option.

The fair appropriation of resources is also a relevant issue here. Time on the radiotherapy machines is a scarce commodity. Using radiotherapy slots to treat patients who do not actually require treatment takes away time from other patients who need to be treated.

Studies have shown that in up to 44% of SCC cases, multiple levels of compression exist, not all of which are symptomatic at the time of diagnosis but many of which cause symptoms later on.<sup>(22)</sup> In our study 62% of the cases had multiple levels of cord compression seen on MRI. For CT scan to replace MRI, it should demonstrate all of the levels of cord compression that MRI does. In this study, it was found that 69% of patients would receive treatment covering all levels of spinal cord compression if oncologist reviewed CT scan was used to diagnose and guide the treatment of this condition. Therefore, over 30% of patients would not have all levels of spinal cord compression treated. As previously mentioned, the consequences for patients with this condition who are not appropriately treated are too dire to undertreat such a large percentage of the patient population.

## Future Research Opportunities

To our knowledge, this is the first study which has compared oncologist reported CT scan with radiologist reported MRI to detect spinal cord compression. Although these results suggest that radiation oncologist reported CT scans are not sufficient for the diagnosis and treatment of spinal cord compression, other important questions were raised which could form the basis for future studies. Is CT scan not sufficient in this setting or are oncologists not skilled enough to interpret the CT scans? Would CT scans reported by radiologists be better? A study performed at St Georges Hospital in London assessed the usefulness of radiologist reported CT for triaging patients with suspected spinal cord compression and found that the agreement between CT and MRI was high.<sup>(16)</sup> There may be value in doing a study which assesses the accuracy of radiologists using CT scan to investigate spinal cord compression.

It was also noted that some doctors scored significantly better than others. The participants were not asked to specify the criteria they had used to define SCC. It is possible that some of the doctors may have used overly stringent diagnostic criteria to determine the presence of SCC? If this was the case, additional radiology training may improve the oncologists ability to assess CT scans for cord compression? This may be a research question for future studies.

### Study Limitations

This was a small study with only eight doctors participating. The range of correct answers varied greatly from doctor to doctor. One participant's performance could therefore have strongly affected the overall study results.

It is postulated that participation of neuro-oncologists who have extensive experience in assessing the spine radiologically may have improved the overall results.

The study did not include enough participant to draw statistically significant conclusions. When using a research nomogram to calculate required sample sizes for sensitivity and specificity calculations for the disease prevalence found in our study, a value of approximately 100 participants is required to prove a sensitivity of 95%. It is possible that improved sensitivity and specificity outcomes would have been obtained with a larger sample size.

Some participants left questions unanswered or did not answer questions fully. It is not known whether this occurred because time was an issue, because the answer was unknown, or merely as an oversight. The unanswered questions were left out of the calculations. The questions which were answered incompletely were marked as incorrect. Leaving unanswered questions out of the data analysis may have introduced bias favouring the results for CT scan.

The multiplanar reconstruction algorithms used may not have been of the requisite resolution. If the images were viewed using diagnostic reconstruction software and diagnostic workstations, the questions may have been answered better and the results may have improved.

The questionnaires were answered during breaks in the normal working day and time pressure may have influenced the quality of the answers. It is possible that if the questionnaire was shorter or if the participants had been allocated dedicated time to participate in the study, the questions may have been answered better.

The significantly larger proportion of true positive test results than true negative results may have introduced bias if whilst assessing multiple scans with obvious pathology, participants become conditioned to see and confident to diagnose other positive results.

False positive and false negative answers to question one (Is SCC present?) by default were scored incorrectly for question two (Where would you treat?). It is possible that if doctors were informed that there was a SCC, they would have been

able to use the CT scan to correctly treat the patient. Thus the results for question two would have been negatively affected by the inclusion of doctors who incorrectly responded to question one. However, this was determined to more closely represent a true clinical setting, where CT would be used sequentially to diagnose and then treat the patient.

## **Conclusion**

The results of this study suggest that CT scan reported by radiation oncologists should not be used to replace radiologist reported MRI for the diagnosis and management of malignant spinal cord compression in environments where MRI is available. Although oncologist reviewed CT scan was shown to have a sensitivity comparable to MRI, its relative accuracy was not sufficient for planning of radiotherapy. In nearly a third (31%) of assessments, the use of CT scan resulted in a geographical miss of the level which contained the cord compression. This would translate into these patients receiving incorrect treatment, thus suffering the consequences of spinal cord compression whilst enduring the side effects and risks of radiotherapy.

In less than half of the cases, doctors reported feeling confident using a CT scan to diagnose and treat these patients. In just over half of the cases, doctors reported that they would change their treatment plan after seeing the reported MRI scan. These results suggest that doctors believe that they are better able to treat spinal cord compression effectively when using an MRI.

However, in view of the level of benefit which may be derived using this alternative approach for the diagnosis of spinal cord compression in a resource-constrained setting, it is strongly urged that further research is done. Possibly, with a larger sample size, the use of better reconstruction software and further training of radiation oncologists in the field of diagnostic radiology, different results may be obtained.

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