Automated Detection of Sclerotic Metastases in the Thoracolumbar Spine at CT¹

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Purpose:

To design and validate a computer system for automated detection and quantitative characterization of sclerotic metastases of the thoracolumbar spine on computed tomography (CT) images.

Materials and Methods:

This retrospective study was approved by the institutional review board and was HIPAA compliant; informed consent was waived. The data set consisted of CT examinations in 49 patients (14 female, 35 male patients; mean age, 57.0 years; range, 12–77 years), demonstrating a total of 532 sclerotic lesions of the spine of greater than 0.3 cm³ in volume, and in 10 control case patients (four women, six men; mean age, 55.2 years; range, 19–70 years) without spinal lesions. CT examinations were divided into training and test sets, and images were analyzed according to prototypical fully-automated computer-aided detection (CAD) software. Free-response receiver operating characteristic analysis was performed.

Results:

Lesion detection sensitivity on images in the training set was 90%, relative to reference-standard marked lesions (95% confidence interval [CI]: 83%, 97%), at a false-positive rate (FPR) of 10.8 per patient (95% CI: 6.6, 15.0). For images in the testing set, sensitivity was 79% (95% CI: 74%, 84%), with an FPR of 10.9 per patient (95% CI: 8.5, 13.3). False-negative findings were most commonly (37 [40%] of 93) a result of endplate proximity, with 32 (34% of 93) caused by low CT attenuation. Marginal sclerosis caused by degenerative change (174 [28.1%] of 620 actual detections) was the most common cause of false-positive detections, followed by partial volume averaging with vertebral endplates (173 [27.9%] of 620) and pedicle cortex parallel to the axial imaging plane (121 [19.5%] of 620).

Conclusion:

This CAD system successfully identified and segmented sclerotic lesions in the thoracolumbar spine.

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Computer-aided detection (CAD) techniques and algorithms for radiologic applications are rapidly growing in scope and sophistication (1,2). In computed tomographic (CT) colonography, mammography, and thoracic CT imaging, the potential for CAD to help increase the detection sensitivity for polyps (3), improve the sensitivity for cancer detection and the accuracy for lesion classification in mammography (4,5), and to enhance reader performance in pulmonary nodule detection and assessment of likelihood of malignancy (6,7) has been previously demonstrated.

Bone metastases affect approximately 400 000 patients per year in the United States (8). Breast and prostate cancer together are thought to account for more than 80% of these bone metastases (9). Early detection of bone metastases is important clinically, as the prognosis can change and the treatment regimen can at that point be altered from one of curative therapy to one of palliative treatment (10).

Traditionally categorized as sclerotic or lytic, metastatic bone disease is now thought to exist as a continuum and may in fact interconvert as part of its natural history (11,12). Both lytic and sclerotic metastatic disease can act to biomechanically weaken bone. In the case of sclerotic metastases, this occurs via irregularly mineralized and disorganized matrix produced as woven bone (13–16). Fractures in pathologically weakened bone occur most commonly in the spine in the prototypical example of sclerotic metastases owing to prostate cancer (14).

The morbidity associated with solid tumor metastasis to the skeleton is

frequent and often debilitating, with secondary skeletal complications (skeletal related events) occurring in approximately 50% of patients (8). Overall, the spine is the most frequent location for skeletal metastases (17).

CT is a routine imaging modality involved in the detection and surveillance of many types of cancer. Detection of bone metastases at CT can be a challenge, with potential lesion oversight if presentation is subtle or if a lesion is unexpected, as when the radiologist interpreting body CT images has not been directed in their search. Additional confounding factors for lesion detection may include bone window underusage (18) and restricted time for image assessment. Within the skeleton, the spinal column is an anatomically intricate structure that may be more challenging to evaluate.

A potential solution to the challenge of detecting subtle or unexpected pathologic findings is the creation of automated secondary “shadow” readers, or CAD systems, which analyze images in parallel to the radiologist. These shadow readers should have the ability to facilitate rapid and accurate assessment of important or high-risk subsets of the CT data, such as data on spinal morphologic characteristics, and alert the interpreting radiologist when potential lesions are detected.

Automated detection of lytic lesions of the spine on CT images with CAD has undergone preliminary assessment in a previous work (18). In addition, preliminary study on the feasibility of CAD of vertebral column metastases at magnetic resonance (MR) imaging and preclinical animal studies of

semiautomated segmentation of mixed spinal metastases at multimodal micro-CT and micro-MR imaging have been reported (19,20). The purpose of this study was to design and validate a computer system for automated detection and quantitative characterization of sclerotic metastases of the thoracolumbar spine on CT images.

Materials and Methods

Patient Population

The study was approved by our institutional review board (National Institutes of Health, Bethesda, Md) and was compliant with the Health Insurance Portability and Accountability Act. Informed consent was waived, as the study was conducted as a retrospective analysis of scans from examinations performed as part of prior clinical care.

An automated search of our institution's radiology information system database (RadNet; Cerner Millennium, North Kansas City, Mo) was performed

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Abbreviations:

CAD = computer-aided detection
CI = confidence interval
FP = false-positive
FPR = FP rate
FROC = free-response receiver operating characteristic
SVM = support vector machine
3D = three-dimensional
2D = two-dimensional

Author contributions:

Guarantors of integrity of entire study, J.E.B., R.M.S.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, J.E.B., J.Y., T.S.W., R.M.S.; clinical studies, J.E.B.; experimental studies, J.Y., H.E.M.; statistical analysis, J.E.B., J.Y., T.S.W., H.E.M., R.M.S.; and manuscript editing, J.E.B., J.Y., R.M.S.

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Conflicts of interest are listed at the end of this article.

Advances in Knowledge

- A computer-aided detection (CAD) system has been developed for detection and quantitative characterization of sclerotic lesions of the thoracolumbar spine imaged at CT.
- This CAD system demonstrates 79% sensitivity for lesion detection, with a rate of false-positive occurrence of 10.9 per patient.

Implications for Patient Care

- This CAD system may be capable of assisting radiologists by acting as an automated secondary reader for detecting sclerotic lesions in the spine.
- This CAD system automatically generates tumor volumetrics, which may be useful in assessment of serial change and in guiding therapy.

Table 1

Primary Cancer Origin in 59 Training and Testing Set Patients

Cancer Type	No. of Patients
Prostate cancer	33
Lung cancer	5
Breast cancer	5
Alveolar soft part sarcoma	3
Thyroid carcinoma	2
Ovarian cancer	3
Ewing sarcoma	2
Pituitary cancer	1
Thymic cancer	1
Gastric sarcoma	1
Hodgkin lymphoma	1
Metastatic carcinoid tumor	1
Pheochromocytoma	1

by using the application Radiology Report Search. Radiology information system search parameters specified the imaging modality as CT or CT/positron emission tomography and searched dictated reports for the free-text keywords of “spine” AND “sclerotic” AND/OR “osteoblastic.” A total of 1927 reports were returned from this search (Fig 1).

One author (J.E.B.), a fellowship-trained board-certified musculoskeletal radiologist with 5 years of experience, reviewed dictated reports retrieved from the search. Examinations with results that were reported as positive and negative for evidence of sclerotic metastatic disease of the spine were partitioned into case (examinations with positive results) and control (examinations with negative results) groups. CT scans from the resulting study sets were then manually reviewed on the hospital picture archiving and communication system (Carestream Health, Rochester, NY). Exclusion criteria were applied during the picture archiving and communication system review (Fig 1). Fifty nonexcluded consecutive patients with studies demonstrating one or more sclerotic lesions of the spine were selected to compose the case set. However, one study was later screened out from analysis by the CAD system during the segmentation process, apparently owing to pediatric stage bone development morphologic features. The

Figure 1

Figure 1: Standards for Reporting of Diagnostic Accuracy chart. PACS = picture archiving and communication system, pts = patients, RIS = Radiology Information System.

Table 2

CT Scanners and Protocols

Scanner Type	No. of Channels	No. of Cases	Reconstructed Section Thickness (mm)*
LightSpeed QX/i; GE Healthcare, Waukesha, Wis	4	2	5
LightSpeed Ultra; GE Healthcare, Milwaukee, Wis	8	11	5
LightSpeed Ultra; GE Healthcare, Milwaukee, Wis	8	1	3.75
LightSpeed Ultra; GE Healthcare, Milwaukee, Wis	8	1	2.5
LightSpeed Discovery ST; GE Healthcare, Waukesha, Wis	8	1	5
Brilliance 64; Philips Medical Systems, Bothell, Wash	64	21	5
Brilliance 64; Philips Medical Systems	64	1	3
LightSpeed VCT; GE Healthcare, Waukesha, Wis	64	1	5
Sensation 64; Siemens Medical Systems, Malvern, Pa	64	1	5
Aquilion One; Toshiba Medical Systems, Otawara, Japan	64	1	5
Somatom Definition; Siemens Medical Systems	128	17	5
Somatom Definition; Siemens Medical Systems	128	1	3

* All studies were performed with helical CT, and images were reconstructed with a soft-tissue kernel.

data set consisted of CT examinations in 49 patients (14 female, 35 male patients; mean age, 57.0 years; range, 12–77 years), with a total of 532 sclerotic lesions of the spine of greater than 0.3 cm³ in volume. Ten consecutive patients (four women, six men; mean age, 55.2 years; range, 19–70 years) with extraspinal sclerotic metastases but no evidence of sclerotic lesions in the spine were selected to compose the control case set of patients. The date of service for examinations selected ranged from

October 2007 to August 2010. Therefore, 59 patients were included in this investigation. The medical records of these patients were reviewed for demographics and origin of patient's diagnosed primary cancer (Table 1).

Image Acquisition

CT examination technique varied according to the scanner used and date of the examination (Table 2). CT scans of the chest, abdomen, and pelvis were obtained in 55 patients, CT scans of

Figure 2

Figure 2: Flowchart of CAD methods. *Density* = attenuation, FP = false-positive, FROC = free-response receiver operating characteristic, SVM = support vector machine, TP = true-positive.

the abdomen and pelvis were obtained in three patients, and CT scans of the chest and abdomen were obtained in one patient. Fifty-seven of 59 patients received intravenous contrast material as part of their examination. The contrast agent was administered (iopamidol injection 61%, Isovue-300; Bracco Diagnostics, Princeton, NJ) to 53 patients in volumes ranging from 40 mL ($n = 1$) to 130 mL ($n = 41$), with one patient receiving 125 mL of iopamidol injection 76% (Isovue-370; Bracco Diagnostics), and one receiving 110 mL of iohexol, with an iodine content of

Figure 3

Figure 3: Spine segmentation results in a 66-year-old patient with prostate cancer. Illustration of the first step in the CAD system image processing algorithm. Left: Automated stripping of surrounding anatomy (including ribs) from the vertebrae is performed on axial CT images by the segmentation software, followed by 3D reconstruction of the spine. Right: Automated identification of the spinal canal is performed as part of this process to assist in isolation and identification of the vertebrae by the segmentation software. Spinal canal here is marked in blue (spinal canal set as translucent at left).

46.36% (Omnipaque-300; GE Healthcare, Princeton, NJ). The contrast agent type and dosage were not available in two of 57 patients.

Lesion Identification

Study images were downloaded in noncompressed Digital Imaging and Communications in Medicine format. Images were reviewed by three fellowship-trained board-certified radiologists, with 5 years (J.E.B.), 17 years (R.M.S.), and 20 years (E.C.J.) of experience, for consensus agreement,

with electronic location marking and segmentation of the lesions. Large heterogeneous sclerotic regions that appeared to be either an amalgam of inseparable smaller-component sclerotic lesions or a single heterogeneous lesion were location marked and segmented as a single lesion. Manual segmentation was performed over the three-dimensional (3D) extent of each lesion, with use of in-house software with a bone window setting (21). After manual segmentation of the lesions with electronic boundary marking, in-house software was used to generate quantitative data in regard to lesion location, volume, and attenuation for comparison with CADs. CT examinations were then partitioned into training and testing sets. The manually segmented lesions were used as the reference standard in this investigation.

CAD Methods

A simplified flowchart of the methods is shown in Figure 2. Initial segmentation of the spine was accomplished by using attenuation threshold levels and region growing. Morphologic operations were used to refine the segmentation, and spinal canal extraction was performed. The spine was then partitioned into 3D vertebral models for division of disk spaces, and vertebrae were partitioned into separately segmented regions of interest (Fig 3) (22).

Once segmentation was achieved, the computer analyzed the spine on sequential axial CT images with a lesion detection algorithm (watershed algorithm) (21). The CAD system processes each vertebra in its entirety (vertebral body, pedicles, laminae, and spinous processes) as part of the initial watershed detection process. The watershed algorithm divided the vertebrae into smaller subregions, on the basis of attenuation differences. Subregions with mean attenuation greater than that of all adjacent subregions were then defined as preliminary detection candidates. As the watershed algorithm tends to oversegment images, an algorithm utilizing graph cuts and threshold levels was applied to merge preliminary detection candidates with abutting

Figure 5

Figure 5: Merging of a candidate lesion, 2D to 3D in same patient and spinal level as in Figure 4. **(a)** Original CT images (top), computer-segmented 2D detections (middle, green), and manually segmented lesions (bottom, blue) on adjacent axial sections. Individual red pixel on each axial section is the CAD system detection mark. Red on images in middle represents other CADs in same vertebra. **(b)** Three-dimensional lesion (dark green) after merging of the axial 2D detections.

Figure 4

Figure 4: Lesion detection and 2D merging algorithm revealed a T12 vertebral body lesion in a 70-year-old patient with prostate cancer. **(a)** Original axial CT image, with heterogeneous sclerotic lesion or conglomeration of sclerotic lesions. **(b)** Watershed segmentation of axial CT cross section before 2D merging. **(c)** Lesion segmentation after 2D merging. **(d)** Axial CT image with merged 2D lesion detection in red.

subregions of similar attenuation (Fig 4) under the assumption that they may represent a single heterogeneous lesion or a conglomeration of multiple sclerotic lesions. The resulting 2D lesion candidates were then merged into 3D detections (Fig 5) by using connected component analysis. A 3D detection was defined as the largest set of 3D adjacent voxels that belong to some detection by using the graph cuts merger.

The centroid of each detection is used as a seed point for level set segmentation (23). Level sets are evolving contours or surfaces that can expand, contract, or even split or merge (24). For the purposes of segmentation, they are designed to deform so as to match an object of interest and stop at its edges.

For each 3D detection, a set of 25 characteristic features was computed. These features can be broadly divided into categories, such as attenuation, morphologic characteristics (including size and shape parameters), and location, with examples including mean attenuation, volume, and sphericity. These features were then submitted to a filter that only allowed detections whose features were within preset ranges to pass through. This filtering restricted the number of detections allowed to pass through, creating a resultant candidate lesion set.

The lesion classifier used was a committee of SVMs (18,25–28). SVMs project data into high-dimensional feature space, which is divided into true-positive and FP regions by using a hyperplane

(25,26). The hyperplane is then optimized for lesion classification, on the basis of comparison of training and reference standard lesion data sets. The candidate lesion set obtained from detection filtering of the training cases was used for training the SVM committee. During the SVM stage of the CAD algorithm, lesion assessment is limited to the body and pedicles. Candidate lesions that demonstrated spatial volume overlap with the manually marked reference standard lesions were classified as true-positive.

Leave-one-out cross-validation of the classifier system was performed on the training data set, with FROC analysis for decision branch point optimization, resulting in a trained SVM classifier. The trained classifier was then applied to the candidate lesions obtained from processing of the testing case set, to yield the final set of CAD system detections (Fig 6). The per-case analysis time for the CAD system was less than 2 minutes on a standard office desktop computer.

The causes of FP and false-negative detections were evaluated by the three fellowship-trained board-certified radiologists (J.E.B., R.M.S., E.C.J.). FP detections were reviewed, and if an FP detection was found to represent a true lesion, not marked by the radiologists creating the reference standard set but detected by the CAD system, it was manually removed from the FP statistic.

Statistical Analysis

System performance was assessed by using FROC analysis of the data set classifications. The operating point value was used as the diagnostic test criterion for the FROC analysis. Analysis was performed for lesions larger than 0.3 cm³ in volume from the manual segmentation (equivalent to 0.84 cm in diameter of a sphere). Lesions that were smaller than this threshold level for size were excluded from the data set and from further statistical consideration. The FROC curve was generated through a bootstrap strategy; 1000 bootstrap methods were performed to derive the confidence intervals (CIs). The bootstrap method was conducted at the patient level to take into account the correlated data.

The operating point value for the training set was chosen to target a sensitivity of 90% or greater, while maintaining a clinically reasonable FP rate (FPR). Then, this same operating point (or 0.42) was used to calculate sensitivity in the test set. Analysis for significance of sensitivity value differences between the training and testing sets was performed by means of a bivariate χ^2 test. Because of the architecturally complex nature of a number of the structures detected, one manually segmented lesion may correspond to multiple CADs. Thus, a direct one-to-one comparison of individual lesions was not always possible, and a comparison of mean values was performed with all lesions included, gauged as a measure of overall tumor burden. As such, CT attenuation values and mean volumes of the manually performed and computer-performed lesion segmentations were compared by means of a mixed-model analysis of variance, taking into consideration clustering of multiple lesions within individual patients (XLSTAT; www.xlstat.com) (29). A difference with $P < .05$ was considered significant.

Results

A total of 532 sclerotic lesions were electronically location marked and segmented in the ground truth data set of 49 cases, for a mean of 10.9 lesions per patient (standard deviation, 10.8) and a range of 1–59 lesions per patient (Table

Figure 6: Three-dimensional detection filtering and final classification in a 75-year-old patient with prostate cancer. (a) Three-dimensional reconstruction of segmented spine data with ground truth lesions marked in light blue. (b) Initial output of detections (red) from 2D watershed and 3D merging algorithms. (c) Candidate lesions (red) remaining after screening by detection filter. Rejected detections in blue. (d, e) Lesions remaining after SVM classification with cutoff of 0.48 (d) and 0.55 (e) (for comparison). Green = true-positive lesions, red = FP lesions. FP detections here were caused by degenerative change and partial volume averaging of vertebral endplates.

3). The CAD system detected 439 true-positive sclerotic lesions, with a mean of 9.0 lesions (standard deviation, 9.7) and a range of 1–57 lesions detected per patient. All 49 case CT studies accumulated during the manual picture archiving and communication system case review phase of the study were positive for lesions at qualitative visual assessment.

For the bootstrap analysis taking into account the clustering of lesions, the CAD system sensitivity for the training set was 90% (95% CI: 83%, 97%) at an FPR of 10.8 per patient (95% CI: 6.6, 15.0). The testing set sensitivity was 79% (95% CI: 74%, 84%) with an FPR of 10.9 per patient (95% CI: 8.5, 13.3) (Fig 7). The testing and training sets did not demonstrate a significant difference in sensitivity, with a bivariate χ^2 test statistic of 10.9 ($P = .001$).

Examples of FP and false-negative detections are shown in Figure 8 and Figure 9, respectively. There were a total of 15 true lesions detected by the CAD

system, not marked in the reference standard set. At review, these lesions were not included in the reference standard set because of small size and low attenuation in eight (53%), because of low attenuation and location at endplate in three (20%), because of small size in two (13%), because the lesion was in an L5 with sacralization that was thought to be outside the region of interest (segmentation) at ground truth marking in one (7%), and because of inadvertent deletion of one electronic lesion segmentation data file during creation of reference standard set in one (7%). FP detections were most often attributable to degenerative sclerosis (174 [28.1%] of 620 actual detections) and misclassification of vertebral endplate bone cortex lying parallel to the (axial) imaging plane (173 [27.9%] of 620) (Table 4). Other causes are noted in Table 4. There were 93 false-negative findings, with 37 (40%) caused by vertebral body endplate proximity, 32 (34%) caused by low attenuation, 17 (18%) caused by small size, and seven (8%) caused by other reasons,

Table 3

Computer-generated Metrics for Lesion Sets

Clinical Data	Reference Standard Lesion Sets		Computer-detected and Segmented Lesion Sets*			
	Training Cases (<i>n</i> = 17)	Testing Cases (<i>n</i> = 42)	Training Cases (<i>n</i> = 17)		Testing Cases (<i>n</i> = 42)	
			TP Detections	FP Detections	TP Detections	FP Detections
No. of lesions	180	352	163	182	276	453
Volume (cm ³)						
Range	0.3–52.7	0.3–56.9	0.1–32.0	0.08–24.1	0.1–27.5	0.1–25.3
Mean ± SD	5.3 ± 9.2	3.2 ± 6.8	3.8 ± 6.3	2.4 ± 3.2	2.8 ± 3.7	2.2 ± 2.6
Length (cm)						
Range	0.7–8.1	0.8–7.6	1.1–6.7	1.0–7.1	1.0–7.0	0.8–7.7
Mean ± SD	2.4 ± 1.5	2.0 ± 1.2	3.0 ± 1.2	3.0 ± 1.2	3.0 ± 1.1	3.0 ± 1.2
CT attenuation per lesion (HU)						
Range	91.8–878	161–821	288–952	276–785	258–791	235–844
Mean ± SD	523 ± 151	385 ± 102	549 ± 141	455 ± 118	428 ± 101	426 ± 109
SD of the mean CT attenuation per lesion (HU)						
Range	24–322	28–285	41–256	38–240	22–267	13–286
Mean ± SD	175 ± 63	119 ± 50	146 ± 49	124 ± 50	115 ± 49	115 ± 55

Note.—SD = standard deviation, TP = true-positive.

* At operating point of 0.42.

Figure 7

Figure 7: FROC analysis for training and testing sets. Training set FROC curve of SVM performance demonstrates 90% sensitivity (95% CI: 83%, 97%) at FPR of 10.8 lesions per patient. Testing set FROC curve of SVM performance (red) demonstrates 79% sensitivity (95% CI: 74%, 84%) at FPR of 10.9 lesions per patient.

such as the finding was out of the search region.

Quantitative metrics were calculated for both the ground truth lesions and lesions identified with CAD (Table 3). The difference in mean lesion volume between ground truth lesions and lesions identified with CAD was not significant, with an approximate volume difference of 15.5% in the training set (mixed-model analysis of variance, $F = 0.734$, $P = .392$) and a 19.3% difference in the testing set ($F = 0.179$, $P = .672$). The difference in mean lesion CT attenuation (Hounsfield units) between manually

segmented lesions and lesions identified with CAD was 0.5% for the training set ($F = 1.056$, $P = .305$) and 1.7% for the testing set ($F = 13.421$, $P < .0001$).

Discussion

Vertebral metastases may be associated with skeletal related events, including pain, compression fractures, spinal cord compression, and hematopoietic abnormalities (14,17,30,31). Researchers in prior studies have demonstrated diminished functional independence associated with skeletal related events

and reduced survival after pathologic fractures (32–34). Patient outcomes are improved with early detection and treatment of vertebral metastases before the onset of marked morbidities (35,36).

We designed and validated a CAD system that successfully automatically detects and determines the volumes of sclerotic metastases of the thoracolumbar spine on CT images. Test set sensitivity and FPR for probable sclerotic spinal metastases were 79% and 10.9, respectively. The difference in sensitivity between testing and training sets was not significant, which suggests data set independence and generalizability of the CAD system.

Similar to the work in prior CAD research in which lytic bone lesions were assessed (18,21), this work focused on CAD of lesions on CT images, utilizing support vector machine lesion classification. In contrast to the work in prior studies, the sclerotic bone lesions in this work were relatively more heterogeneous in attenuation and less insular. There were more lesions in this case set, compared with the lesions in the prior lytic lesion study (18). The increased level of disease

Table 4**Causes of FP Detections**

Group	Degenerative Sclerosis	Volume Averaging at Pedicle Cortex	Cortex of Vertebral Endplate	Sclerotic Intravertebral Channel Wall Basivertebral Veins	Sclerotic Wall Schmorl Node	Other*	Out of Search Region
All cases ($n = 620$) [†]	174 (28.1)	121 (19.5)	173 (27.9)	40 (6.4)	20 (3.2)	25 (4.0)	67 (10.8)
Training set	41	47	48	4	5	8	19
Testing set	133	74	125	36	15	17	48

Note.—Of a total of 635 false-positive detections, 15 appeared to be true-positive but not labeled by radiologists, for a total of 620 actual FP detections.

* Other included bone island, physal scar, et cetera.

[†] Numbers in parentheses are percentages.

Figure 8

Figure 8: FP detections. Axial CT sections demonstrate FP detections (marked with a red pixel) owing to the following: (a) cortex of neuroforamen, (b) cortex of vertebral endplate, (c) combination of neuroforaminal cortex and neurocentral synchondrosis scar, (d) sclerotic intraosseous channel wall of basivertebral neurovascular bundle, (e) degenerative sclerosis of an anterolateral osteophyte, (f) bone island, and (g) sclerotic Schmorl node margin.

Figure 9

Figure 9: False-negative detections. Axial CT sections show false-negative detections (marked with a red pixel) owing to the following: (a) low CT attenuation and (b) small volume, and (c) lesion is near vertebral body endplate and has low attenuation.

complexity in this study necessitated an increased level of algorithmic complexity for lesion detection and feature computation compared with that in the prior analysis. This increased software complexity was partially accomplished by means of incorporation of newer techniques for 2D candidate merging, as well as by means of SVM classifier training on 3D features (compared with 2D SVM feature training, performed in the prior lytic lesion work). Ten patients without sclerotic spinal metastases were used in the software training and testing phases of this work

to mimic a more realistic clinical scenario. Finally, quantitative metrics for lesion volume and CT attenuation were calculated for comparison of the CAD system and manually performed lesion characterization in this study.

The difference in mean lesion volume between reads with experienced observers in consensus and the CAD reads was not significant. Of particular interest, manual tracing of each lesion margin for electronic segmentation, with each lesion typically extending over multiple axial image sections, required tens of hours of radiologists' time. The

CAD system was able to automatically analyze each case in less than 2 minutes on a standard office desktop computer.

Often when training a classifier, the classifier is trained by feature selection (37). However, in this work, preliminary design testing for the feature selection optimization process indicated no benefit to feature selection. All features were found to be highly relevant to the problem, and thus feature selection was thus not incorporated into the final algorithm.

There were several limitations in case and lesion selection. The first limitation was absence of direct

pathologic confirmation of the type of the cell of origin of the lesions. As in the prior CAD lytic lesion study, biopsy of metastatic lesions is not typically performed unless confirmation of cellular origin is required during initial diagnosis or local therapy. All patients chosen for this study had a confirmed primary tumor, and in patients who were suspected of having secondary lesions, the lesions were assumed presumptively to be metastatic disease. The second limitation was selection bias, as patients selected were those in whom radiologists (not participating in this study) had already noted and dictated reports affirming the presence of sclerotic spinal metastatic disease. These lesions may also represent a biased sample as a more visually obvious cohort, and the CAD system may be trained toward the detection of more overt lesions. A third limitation was that examinations used in this study were chosen with a CT technique to model standard body imaging series which would be performed for patients without known bone metastasis, predominantly with 5-mm section thickness. With this relatively large section thickness, small lesions may be missed owing to a partial volume averaging artifact. Fourth, as this was a preliminary study for proof of concept, only moderate or larger lesions of greater than 0.3 cm³ were assessed. Given the lack of characteristic appearance for lesions smaller than 0.3 cm³, this was deemed an appropriate starting point. However, future work may include detection and assessment of small or early lesions where alternative imaging modalities are available to increase the confidence in the cause of the lesion.

In addition, there were limitations in the CAD system design. First, the bounding region for the CAD system sclerotic lesion search was limited to the body and pedicles of the vertebrae. This anatomic simplification was believed to be justified; because this work was intended as a preliminary proof of concept study, it has been shown previously that the primary loci for early metastatic

spread to the vertebrae are in the vertebral body and pedicles, and most of the volume of each vertebra is constituted by these regions (38–40). Bounding box inclusion of the vertebral body and pedicles thus assesses the most likely regions of early metastatic tumor involvement. Future work could include the laminae, transverse and posterior spinous processes, for a more complete evaluation, and characterization of sclerotic tumor burden. Second, the FPR is relatively high. Two of the three most common causes (volume averaging of cortex at vertebral endplates and pedicles) may be decreased by a more sophisticated segmentation algorithm design, and the third (degenerative sclerosis) may be decreased by an addition of an algorithm, now in design stage, designed to detect degenerative change of the vertebrae. Elimination of these three causes of FPs would eliminate three-quarters of FP detections. Third, images reconstructed with a soft-tissue kernel were used to decrease the effect of image noise on software performance. Future design may include increased robustness in the presence of image noise. Finally, only sclerotic lesions were addressed because of the complexity of the problem of detection and analysis of heterogeneous sclerotic lesions.

In conclusion, we described a CAD system that can detect sclerotic metastases of the thoracolumbar spine on CT images. Some common causes of FP and false-negative detections were discussed to guide further CAD algorithm development.

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