Computer Aided Lytic Bone Metastasis Detection Using Regular CT Images

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ABSTRACT

This paper presents a computer aided detection system to find lytic bone metastases in the spine. The CAD system is designed to run on routine chest and/or abdominal CT exams (5mm slice thickness) obtained during a patient’s evaluation for other indications. The system can therefore serve as a background procedure to detect bone metastases. The spine is first automatically extracted based on adaptive thresholding, morphological operation, and region growing. The spinal cord is then traced from thoracic spine to lumbar spine using a dynamic graph search to set up a local spine coordinate system. A watershed algorithm is then applied to detect potential lytic bone lesions. A set of 26 quantitative features (density, shape and location) are computed for each detection. After a filter on the features, Support Vector Machines (SVM) are used as classifiers to determine if a detection is a true lesion. The SVM was trained using ground truth segmentation manually defined by experts.

Keywords: Computer Aided Detection, bone metastasis, spine segmentation

1. INTRODUCTION

Bone metastasis occurs when cancer cells from the primary tumor relocate to the bone. Bone metastases can cause great morbidity including debilitating pain and pathologic fractures; spinal metastases can produce cord compression and severe neurologic impairment [1]. Seventy percent of bone metastases involve the axial skeleton (ribs, spine or sacrum), while the remainder involve long bones. Bone metastases have been characterized as osteolytic (lytic) or osteoblastic [2]. This classification represents two extremes of a continuum in normal bone dys-regulation. Patients can have both types of bone metastases. Lytic lesions can weaken the bones and increase the risk of bone fracture and other problems. Lytic lesions are the focus of this investigation.

The spinal column constitutes the central axis of the human body and is an essential part of the skeleton. It supports the upper body and protects the spinal cord. Early diagnosis of these spinal metastases is important as treatment before the development of significant morbidities improves outcomes. Figure 1 shows one example of lytic bone metastases in the spine.

The main imaging techniques used to diagnose bone tumors are conventional Xrays, CT, MRI, and isotope bone scans. While MRI is the most used and sensitive imaging tool, CT provides the best resolution and specificity [3]. Tens of thousands of routine chest and abdominal CT’s are acquired every day to evaluate patients for various indications. These CT images are generally underutilized. Our CAD technique is applied to the routine CT images so that it can be used as a background procedure and report suspicious abnormalities to the radiologists.
In this paper, we introduce a novel CAD system to find lytic metastases in the spine. Section 2 presents the overview of our method. Section 3 presents the automated spine segmentation method. Section 4 describes the metastasis detection and classification method. In section 5, we validate this system on a set of known cases and show CAD to be feasible with a reasonably low rate of false positives. Finally we provide some discussion in section 6.

2. MATERIAL AND METHOD OVERVIEW

Example images are shown from patients scanned using routine chest/abdominal CT protocol. The slice thickness was 5mm and the data set consisted of an average of 120 images. Our method has two stages: spine segmentation stage and bone metastases detection stage. Figure 2 shows the flow chart of our method. In the spine segmentation stage, first the initial segmentation is obtained, then the spinal canal is extracted, at the end the segmentation is refined based on the spinal canal. In the bone metastasis detection stage, first the potential metastasis regions are detected, then quantitative features are computed, these features are then passed through a filter and a classifier to determine if a detection is a true lesion.

3. AUTOMATED SPINE SEGMENTATION

Automated spine segmentation is difficult due to the articulated structure of the vertebrae and their dense contact with ribs and other organs, especially in the thoracic spine [4]. Bone abnormality such as metastasis creates holes and gaps in the vertebrae, which also complicates the segmentation. Simple methods such as thresholding and region growing are usually not sufficient. Due to the thick slices and partial volume effect, segmentation on routine CT image faces even greater challenges.
3.1 Initial segmentation and spine localization

Initial segmentation and spine localization is achieved by simple thresholding and region growing. Bone structures have higher CT value than other soft tissues. We apply a threshold of 200 HU to mask out the bone pixels. Then a connected component analysis is conducted on the bone mask and the largest connected blob in the center of the image is retained as the initial spine segmentation. A bounding box is computed on each slice and used as the spine window. All following operations are conducted inside the spine window.

3.2 Spinal canal extraction

The spinal canal links all vertebrae into a column and houses the spinal cord. On 2D slices, the spinal canal appears to be a low intensity oval region surrounded by vertebral structures (spinal process, vertebral body, pedicle and transverse processes) (Figure 3a, 3b). The extraction of the spinal canal is essential in accurately localizing the spine and forming the column.

We first apply a threshold of 76 HU to extract all potential spinal canal regions within the spine window. A connected component analysis is conducted to generate potential spinal canal region. After that, a filter on the size and location is applied to each region. Figure 3b shows the canal candidates. The false candidates are typically bone metastasis (figure 3c) and regions caused by partial volume of inter-vertebral discs (figure 3d).

To locate the true spinal canal, we propose a method based on directed graph search. We first build a directed acyclic graph (DAG) from the canal candidates. The DAG is illustrated in figure 4. The graph $G(V, E)$ is a structure that consists of a set of nodes $V$ and a set of directional edges $E$. A node is one canal candidate. A directional edge $<n_1, n_2>$ connects two nodes $n_1$ and $n_2$ on adjacent slices, where the weight of $<n_1, n_2>$ is computed as the overlap of $n_1$ and $n_2$, as in Equation 1:

$$
weight(<n_1, n_2>) = \frac{\bigcap (n_1, n_2)}{\bigcup (n_1, n_2)}
$$

$$
\bigcap (n_1, n_2) = \{x_i, y_i \in n_1 \text{ and } x_i, y_i \in n_2\}
$$

$$
\bigcup (n_1, n_2) = \{x_i, y_i \in n_1 \text{ or } x_i, y_i \in n_2\}
$$

An edge only exists when its weight is greater than 0 (two nodes overlap). DAG has sources on the first slice and sinks on the last slice. A directed graph searching algorithm [5] is applied to find the longest path from source to sink, which is the spinal canal in our case. In figure 4, the longest path is marked with red color. The centerline of the spinal canal is then computed and smoothed using a Bernstein spline.

After the spinal canal is extracted, the spine window can be further restrained to a rectangular region surrounding the spinal canal. Any excessive bone outside the spine window can be removed from the segmentation. Since slice thickness is large (5 mm) and bone density is inhomogeneous within and
across patients, segmented regions are usually not connected and have many artifacts. Furthermore, bone metastases can cause gaps along the borders of vertebral bodies and holes inside the bone. Two refinement measures are taken to fine-tune the segmentation. First, mathematical morphological operations are applied to merge disconnected bones and fill small holes inside the bone. Then, a rolling ball transformation [6] is applied to fill gaps along the border.

Figure 5 shows some results for the spine segmentation. Figure 5a is the original image, 5b is the result after initial segmentation, and 5c is the result after spinal canal extraction and segmentation refinement. In the figures, red color indicates the spine region, and blue color indicates the spinal canal.

4. BONE METASTASIS DETECTION AND CLASSIFICATION

After the spine is segmented from the image, potential bone metastases are detected. There are three steps in the detection process: first the suspected metastases region are extracted using a watershed algorithm, then quantitative features are computed and passed through a filter, and finally a classifier is applied to retain the highly suspected lesions (Figure 2).

4.1 Watershed method for detection

The lytic bone metastases appear as a low intensity region surrounded by high intensity regions on a 2D CT image. This makes its extraction a suitable case for the watershed algorithm. The principle of the watershed algorithm [7] is to transform the gradient of a gray level image into a topographic surface. The algorithm punctures holes at the local minimum of the intensity and fills the region with water. Each region filling with water is called a catchment basin. When the water rises, two neighboring basins may merge into one region. The spinal canal resembles a catchment basin in a 2D slice. We adopted the watershed algorithm implementation in ITK [8].

The well known over-segmentation problem of the watershed algorithm is alleviated by merging neighboring basins. Depth of a basin is defined in Equation 2.

\[ d(b) = \text{average}(I(x)), \quad x \in b \]  

(2)
here \( I(x) \) is the image intensity of pixel \( x \) inside the basin \( b \). Suppose \( a \) and \( b \) are two neighboring basins, they will be merged if both conditions in Equation 3 are satisfied

\[
\begin{align*}
|d(b) - d(a)| &< d(c_i) - d(a) + \delta_n, \forall c_i \in N(a), c_i \neq b \\
|d(b) - d(a)| &< d(c_i) - d(b) + \delta_n, \forall c_i \in N(b), c_i \neq a
\end{align*}
\]

(3)

here \( N(a) \) denotes neighbors of basin \( a \), \( \delta_n \) is the merging threshold. After that, all basins that meet the criteria in Equation 4 and surrounded by bone pixels are recorded as potential candidates for the metastases.

\[
d(c_i) - d(b) > \delta_d, \forall c_i \in N(b)
\]

(4)

here \( \delta_d \) is the depth contrast threshold. Figure 5d shows the result of the watershed algorithm and the detections from the watershed algorithm (green region).

### 4.2 Feature computation and filter

After the detections are segmented, quantitative features are computed to characterize the detections and distinguish the true lesions from the false findings. Based on observation and knowledge about the bone metastasis, we devised a set of 26 quantitative features in three categories: location, shape and density. Table 1 lists all the features.

#### Table 1. Quantitative features for bone metastasis

<table>
<thead>
<tr>
<th>Feature Category</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Shape</strong></td>
<td>area, perimeter, primaryAxis, secondaryAxis, aspectRatio, sphericity, compactness, roundness, shapeComplexity_f1, shapeComplexity_f2, shapeComplexity_f12, borderThickness, outerBorderRatio</td>
</tr>
<tr>
<td><strong>Density</strong></td>
<td>meanDensity, stdevDensity, skewnessDensity, kurtosisDensity, interiorDensity, borderDensity, outsideDensity, outsideDev, contrast</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td>relCoordx, relCoordy, relCoordz, distToBoundary</td>
</tr>
</tbody>
</table>

The shape features are based on the spatial moment of the binary object of the detection [9]. The density features are derived from the statistical moments of the intensity histogram of the segmented region. The relative coordinates of the detection to the center of the spinal canal is used as the location features.

Since a large number of detections are usually generated from the watershed algorithm, feature filters need to be applied to reduce the number of detections and relieve the burden of the classifier in the next step. The filters are designed based on observation of typical bone metastases. The set of filters currently in used are
The feature filters dramatically reduce the number of detections, which makes the training in the classification stage much more efficient and robust.

4.3 Classification

Some false detections closely resemble bone metastases in terms of shape, size and density, so it is almost impossible to separate them just based on linear filters. A non-linear classifier is generally necessary to further reduce the number of false positives. Support Vector Machines (SVM) are a relatively new technique for data classification. It uses hyperplanes in a high dimensional feature space to separate data into different classes [10]. SVMs are trained with a learning system derived from statistical learning theory, and are generalizable to unknown data.

In the training phase, detections are given a class label (metastasis, non-metastasis) to form the feature-class pairs \((x, y)\). Given a training set of \(S\) detections \((x_1, y_1), (x_2, y_2), \ldots, (x_s, y_s)\), for \(p\)-dimensional feature space \(x_j \in \mathbb{R}^p\) and \(y_j \in \{+1, -1\}\), we first define a hyperplane:

\[
f(x) = w^T \phi(x) + b = 0
\]

(5)

here \(w\) and \(b\) are plane parameters, and \(\phi(x)\) is a function to map vector \(x\) into a higher dimensional space. \(K(x_i, x_j) = \phi(x_i)^T \phi(x_j)\) is called the kernel function. We are using radial basis functions as the kernel function, i.e.
To separate two training classes, SVM is employed to solve the following optimization problem:

$$
K(x_i, x_j) = \exp\left(-\frac{\|x_i - x_j\|^2}{\sigma^2}\right).
$$

(6)

To separate two training classes, SVM is employed to solve the following optimization problem:

$$
\begin{align*}
\min_{w,b,c} & \quad \frac{1}{2} w^T w + C \sum_{i=1}^{N} \xi_i \\
\text{subject to} & \quad y_i (w^T \phi(x_i) + b) \geq 1 - \xi_i, \; \xi_i \geq 0
\end{align*}
$$

(7)

Here \( C \) is the penalty parameter. The mechanism of SVM is illustrated in figure 6, where a hyperplane is fit to separate two groups of dots. SVM allows a soft margin on each side of the hyperplane. For each data point, the distance to the margin of hyperplane is computed. If the point is on the correct side of the plane, the distance is 0. The optimization process is to minimize the total distance of all training points. After the hyperplane is determined, the decision function for classification rule can be written as

$$
h(x) = \text{sign}(f(x))
$$

(8)

A new detection \( x \) is declared a polyp if \( h(x) > 0 \), or a non-polyp if \( h(x) < 0 \). The feature values in the SVM are normalized to the range of \([-1, +1]\). The normalization factor is obtained from the training data and applied to the testing data.

SVMs in very high dimensional space may increase the complexity of the model, over-train the data and decrease the generality of the model. Therefore, we break the feature space into subsets of low dimension feature spaces. Each feature vector establishes one SVM, and all SVMs form a committee. We allow overlap of features between different feature subsets. This scheme combines the advantages of using a large number of features and keeping the feature space small for single SVM in the committee. Each member in the committee has one vote for the classification, i.e., if the decision function of the SVM is greater than 0, the vote is ‘yes’, otherwise the vote is ‘no’. The majority vote is used as the decision function of the committee. The committee approach generally produces improved results, provided that the error rate for each member is less than 50%. Figure 6 demonstrates how the SVM committee works. This is a committee of three SVMs. In the first SVM, there are two misclassified data (big square and big circle), but in the second and third SVM, they are correctly classified. By a majority vote, a correct classification is reached.

We developed a progressive feature vector selection method to pick a large pool of highly performing feature subsets. The configuration of the SVM committee is determined by a two-way ANOVA analysis. The details of these techniques can be found in [11]. In our current setup, we have a committee of 7 members, and each member is a 3-feature subset.

### 5. RESULTS AND VALIDATION

The result of our method is shown in Figure 5. It demonstrates the process of segmenting and detecting bone metastases from CT. Figure 5a-5c show the spine segmentation, and figure 5d-5f show the
Figure 7. False position detections
First row is original images, second row is processed images. Detections are marked with green color
a) basivertebral vein; b) partial volume effect; c) gap between vertebra and rib

6. CONCLUSION
This paper presented an automatic method to detect bone metastases in the spine using routine CT images. Our technique overcame the challenge presented by the complex vertebral structure and partial volume effect caused by the thick image slices. Our system is intended to run in the background and provides important and useful information for further analysis. We plan to extend this system to detect lesions in other bones and find mixed and sclerotic lesions in future investigations.

7. ACKNOWLEDGEMENT
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8. REFERENCES