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Automated detection of bone metastatic changes using serial CT scans

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ABSTRACT

Bone metastases resulting from a primary tumor invasion to the bone are common and cause significant morbidity in advanced cancer patients. Although the detection of bone metastases is often straightforward, it is difficult to identify their spread and track their changes, particularly in early stages. This paper presents a novel method that automatically finds the changes in appearance and the progress of bone metastases using longitudinal CT images.

In contrast to previous methods based on nodule detection within a specific bone site in an individual CT scan, the approach in the present study is based on the subtraction between two registered CT volumes. The volumes registered using the proposed weighted-Demons registration and symmetric warping were subtracted with minimizing noise, and the Jacobian and false positive suppressions were performed to reduce false alarms.

The proposed method detects the changes in bone metastases within 3 min for entire chest bone structures covering the spine, ribs, and sternum. The method was validated based on 3-fold cross validation using the radiologists' markings of 459 lesions in 24 subjects and was performed with a sensitivity of 92.59%, a false positive volume of 2.58%, and 9.71 false positives per patient. Note that 113 lesions (24%) missed by the radiologists were identified by the present system and confirmed to be true metastases. Indeed, three patients diagnosed initially as normal, having no metastatic difference, by radiologists were found to be abnormal using the proposed system.

Automatic detection method of bone metastatic changes in the entire chest bone was developed. Weighted Demons, symmetric warping, following false positive suppressions, and their parallel computing implementation enabled precise and fast computation of delicate changes in serial CT scans. The cross validation proved that this method can be quite useful for assisting radiologists in sensing minute metastatic changes from early stage.

1. Introduction

The use of longitudinal computed tomography (CT) has increased in a prospective and follow-up CT study of the nodule changes and metastatic tumor. Bone metastases, which are the spread of cancer from one part of the body to the bone, are quite common and critical issues in staging cancer, causing significant morbidity and mortality, such as pain, fractures, or spinal cord compression. The majority of patients with breast cancer (90%) or prostate cancer (75%) develop bone metastases. In addition, spinal metastases secondary to breast cancer develop toward mixed lesions with a corresponding decrease in lytic lesions (Skrinskas et al., 2009). Although the detection of bone metastases is often straightforward, it is difficult to identify the spread of bone metastases and track their changes, particularly at the early stages. For quantitative readouts of bone metastases from longitudinal CT, practitioners commonly detect the changes in metastatic tumors by comparing each longitudinal CT scan and calculating their volume size manually. Several approaches have been proposed for the detection of metastases. Huang et al. (Huang and Chian, 2012) proposed an automated computer-aided detection (CAD) system to detect vertebral metastases of breast cancer using the texture features and an artificial neural network. In this method, vertebral metastases were identified in the trabecular centrum of the verte-

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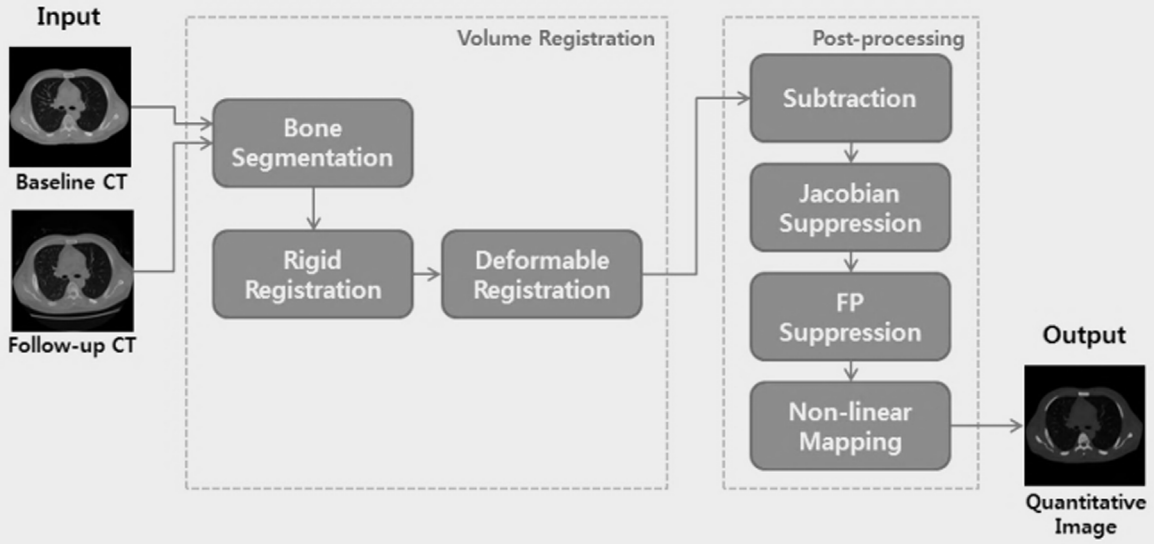

Fig. 1. Flow chart of bone metastatic changes detection algorithm.

bral body detected for each slice, resulting in 86% sensitivity. Wiese et al. (Wiese et al., 2011) introduced a CAD system to aid radiologists in finding sclerotic bone metastases in the spine. This method segments potential lesion candidates in each two-dimensional axial CT image, and eliminates false candidates using a feature filter, resulting in 77% sensitivity at an average of 9 false positives (FP) per case. Yao et al. (Yao Jianhua et al., 2012) suggested a CAD system for detecting sclerotic metastatic bone lesions of the ribs on routine CT studies, with a sensitivity of 75.4% at an average of 5.6 FP per case. Burn et al. (Burns, 2013) used a watershed and merging algorithm to detect lesions and a support vector machine (SVM) classifier to filter out the false positives caused by degenerative changes and partial volume averaging of the vertebral endplates. These approaches required a lesion segmentation technique of a specific bone site in each CT scan. Studies based on multi-modal PET-CT imaging (Beheshti, 2009; Beheshti et al., 2008; Tateishi, 2008) have also been performed, but they are beyond the scope of the present study.

In addition, Hardisty et al. (Hardisty et al., 2007) developed a semi-automated segmentation method to extract the vertebral body and the trabecular centrum in a healthy or metastatic spine using a composition of atlas-based demons registration and level set segmentation, hence enabling a quantitative assessment of vertebral metastases. For visual enhancement, Toth et al. (Toth et al., 2014) recommended the use of a combination of cancellous bone reconstruction and multi-planar reconstructions (MPR) that increased the detection of bone metastases significantly and decreased the interpretation time (a sensitivity of 74% compared to 35% for MPR alone). None of the previous studies could show a sensitivity of 90% or higher at a 10 FP rate. The aim of this study was to enhance the sensitivity rate to more than 90% with the FP rate, which would allow the detection of more true bone metastases and was agreed by clinicians for use in clinical practice. Furthermore, the detection area is limited to the spinal column, which is the most common site of bone metastases, but should include the ribs and sternum as other common sites.

This paper proposes a new automated registration-based method (Fig. 1) to localize changes in sclerotic (blastic) or lytic bone metastases in not just the spine but ribs and sternum using longitudinal CT scans. The method consists of volume registration between the baseline and follow-up scans and post-processings to compute the metastatic changes and to alleviate the false positives.

2. Material and methods

2.1. CT acquisition protocols and subjects

Serial chest inspiration CT scans of 24 patients were used for building a binary classifier to detect bone metastatic changes. The serial CT scans were acquired in a normal dose helical scan (120 kV, 100–330 mAs, standard filter) from a variety of manufacturers and consisted of the baseline and follow-up scans with a gap of 18 ± 12 months. The in-plane resolution was 0.6 mm x 0.6 mm and the slice thickness was 2.5 mm. The image size was 512×512 and the mean number of slices was 120 with a maximum of 160.

2.2. Bone segmentation

Bone segmentation is an important preprocessing step for detecting bone metastatic changes. The bone segmentation was initiated with thresholding (> 1000 Hounsfield unit (HU)), where the HU scale used in the CT numbers was obtained from a linear transformation of the attenuation coefficients measured by a penetrating x-ray beam, and the scale lies in the specific range depending on the penetrated substance (air = −1000 HU, water = 0 HU, bone = 1000 HU), exploiting the high density characteristics of the bone and is followed by selecting the largest 3-D connected region. Bone marrow, which is an internal area of cortical bone, may not be covered with the given threshold of 1000 HU because of its lower HU range. When using a lower threshold for including up to the bone marrow, unwanted soft tissue of the organs of which the HU range is overlapping may also be included. Therefore, to easily enclose the bone marrow, it is filled in by 2-D closing, i.e. dilation followed by erosion, with a 3×3 disk-shaped structuring element and subsequent hole filling morphological operations in each slice. The missed bone with the appearance of lytic metastases with a low intensity range can be enclosed by the aforementioned morphology method, but some cases seen as large indentation were difficult to include. To correct the missed segmentations, the continuity of the segmented voxels in the slice direction was inspected. If the voxels are not segmented but the nearby voxels at the same XY locations in its neighbor slices were segmented, they were deemed to be missing bone segments, and otherwise not bone segments. This process was repeated for up to three neighbor slices above and below.

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