Dual-energy CT-based Assessment of the Trabecular Bone in Vertebrae

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Summary
Background: Osteoporosis can cause severe fractures of bone structures. One important indicator for pathology is a lowered bone mineral density (BMD) – conventionally assessed by dual-energy X-ray absorptiometry (DXA). Dual-energy CT (DECT) – being an alternative that is increasingly used in the clinics – allows the computation of the spatial BMD distribution.

Objectives: Using DECT, the trabecular bone of vertebrae is examined. Several analysis methods for revealing the bone density distribution as well as appropriate visualization methods for detecting regions of lowered BMD are needed for computer-assisted diagnosis (CAD) of osteoporosis. The hypothesis that DECT is better suited than DXA for the computation of local BMD is investigated.

Methods: Building on a model of the interaction of X-rays with bone tissue, novel methods for assessing the spatial structure of the trabecular bone are presented. CAD of DECT image data is facilitated by segmenting the regions of interest interactively and with an Active Shape Model, respectively. The barycentric space of fractional volumes is introduced as a novel means for analyzing bone constitution. For 29 cadaver specimens, DECT as well as DXA has been examined. BMD values derived from both modalities are compared to local force measurements. In addition, clinical data from two patients who underwent DECT scanning for a different reason is analyzed retrospectively.

Results: A novel automated delineation method for vertebrae has been successfully applied to DECT data sets. It is shown that localized BMD measurements based on DECT show a stronger linear correlation (R² = 0.8242, linear regression) to local force measurements than density values derived from DXA (R² = 0.4815).

Conclusions: DECT based BMD assessment is a method to extend the usage of increasingly acquired DECT image data. The developed DECT based analysis methods in conjunction with the visualization provide more detailed information for both, the radiologist and the orthopedist, compared to standard DXA based analysis.

1. Introduction

According to the WHO [1], the lifetime risk for a wrist, hip or vertebral fracture caused by osteoporosis is between 30 and 40% in the developed countries. Osteoporosis is a disease causing a loss of bone mineral density (BMD) that is responsible for about 650,000 fractures a year in the European Union [2]. The WHO defines osteoporosis on the basis of BMD assessment using dual energy X-ray absorptiometry (DXA) [3]. However, these DXA scans have only a low sensitivity, i.e., the fracture risk is high in case of osteoporosis but not negligible at all even if the BMD is normal [1]. One reason for this is the fact that DXA measures an integral bone density including cortical bone – the outer dense shell – and trabecular bone – the inner spongy bone structure. But the latter is known to be metabolically more active and thus more subjected to a decrease of density [4].

One can overcome this problem by employing a 3D imaging modality and restricting the BMD assessment to the trabecular bone. For this, quantitative computed tomography (QCT) has been used in the past [5]. The recently introduced dual-source computed tomography (DSCT) [6] – where two source-detector-pairs are built into the same gantry – allows for a simultaneous acquisition of two image data sets. The two X-ray tubes can operate at different tube energies. Thus, dual-energy computed tomography (DECT) which has been proposed already in the 80s of the last century [7] can easily be performed in the clinical routine using a DSCT scanning device. To our knowledge, this DECT has not been used so far for BMD assessment, although several possible approaches have been proposed already several years ago [8–10].

In this work, we present a novel approach for regional BMD assessment in vertebrae based on DECT image data, employing the method published by Nickoloff et al. [9] for DECT image data acquired with state-of-the-art DSCT technology. We extend that global BMD computation to a regional method which provides the spatial BMD distribution.
2. Methods

We base the BMD assessment on two DECT image data sets acquired at two different peak tube energies. Due to their simultaneous acquisition, both data sets are aligned. The evaluation is based on two different sets of data. The first one comprises DECT and DEXA data as well as force measurements for 29 cadaveric specimens of three different patients. The second set of data stems from two patients who underwent DECT for other reasons than osteoporosis diagnosis.

2.1 Nickoloff Model

For the computation of the BMD, we make use of a method proposed by Nickoloff et al. [9]. This approach accounts for the five major substances of the trabecular bone (Fig. 1). The normalized overall volume is expressed as the sum of the three fractional volumes: the volume occupied by the matrix material $V_{TB}$, the volumes of adipose tissue $V_T$, and the volumes of non-adipose tissue $V_F$. Hence, we have the relation $V_T = 1 - V_{TB} - V_F$. The two remaining unknowns $V_{TB}$ and $V_F$ can be assessed by the two available measurements:

\[
\begin{align*}
\chi^{\text{Low}} &= (\mu_{\text{Low}} - \gamma^{\text{Low}} g) \cdot V_{TB} + \\
(\beta_{\text{Low}} - \gamma^{\text{Low}} g) \cdot V_T + \gamma^{\text{Low}} g + \delta + \varepsilon \\
\chi^{\text{High}} &= (\mu_{\text{High}} - \gamma^{\text{High}} g) \cdot V_{TB} + \\
(\beta_{\text{High}} - \gamma^{\text{High}} g) \cdot V_T + \gamma^{\text{High}} g + \delta + \varepsilon
\end{align*}
\]

The variables in the above equations are known density values and energy dependent values, respectively. Detailed information about them can be found in [9] and [11]. The values $\chi^{\text{Low}}$ and $\chi^{\text{High}}$ are averaged CT numbers (i.e., intensity values) for the voxels representing the region where BMD values are computed.

2.2 Interactive Delineation of the Trabecular Bone for Cadaveric Data Sets

In order to restrict the computation to the trabecular bone, this region has first to be delineated in one of the data sets. For this, we employ an interactive segmentation approach recently introduced [12]. Initial templates for three different regions – the complete trabecular bone of the vertebra, mainly the vertebral body, and a bowling pin shaped region where a pedicle screw is placed – are obtained by manually drawing contours in a stack of 2D slices containing an arbitrary vertebra. These regions (Fig. 2) represent three clinical scenarios: examination of the whole vertebra, DXA-like examination of only the vertebral body, and prediction of pedicle screw stability. A mesh representation of each of the labeled regions is created using the Marching Cubes [13] algorithm which is subsequently refined to contain evenly distributed vertices. It serves then as a template for the segmentation of a specific region in any vertebra that should be examined.

For this, the template is roughly aligned with the image data by the user. Afterward, the mesh can be locally deformed by pulling the boundaries of the mesh toward the desired position (Fig. 3). The exerted force at a specific vertex is propagated to adjacent nodes using a 3D Gaussian kernel.

If the user is satisfied with the delineation of the trabecular region, a mask image is created where all voxels inside the resulting mesh are labeled. This is a third image data set to be used in the subsequent steps.

2.3 Semi-automatic Labeling for Real Patient Data Using an Active Shape Model

Even though the interactive delineation of the trabecular bone is an efficient approach for single cadaveric specimens, an application of this rather time-consuming approach to data from real patients (containing multiple vertebrae) requires an automated approach. For labeling the real patient data, we use the segmentation algorithm Active Shape Model (ASM) by Cootes et al. [14], which uses a priori knowledge about the vertebral shape. This prior knowledge is incorporated by means of a Statistical Shape Model (SSM). The SSM is learned by applying a Principal Component Analysis (PCA) to a set of training vertebrae.

Each training vertebra was extracted from an expert segmentation using the Marching Cubes algorithm [13], which means that the training shapes have in general a different number of points and no index correspondence. A prerequisite for applying PCA is to establish correspondence between the input shapes: Each training vertebra has to be represented by exactly N surface points, and points with the same index on different shapes must represent the same anatomical location.

2.4 Establishing Point Correspondence

For this correspondence establishment, we use the parameterization-based approach recently introduced by Becker et al. [15]. We first choose a reference mesh which is cut along two loops – using the algorithm of Erickson and Whittlesey [16] – in order to be able to flatten it to a rectangle. The parameterization is done using the method of Tutte...
Followed by a distortion reduction [18]. The elements of the remaining training set are treated as follows: First the reference loops are propagated such that we cut approximately along the same paths for all training vertebrae. On the parameter space we establish correspondences using a combined energy. Its first term is based on point-to-point distances and the second term is Degener’s energy [18] which is used for reducing the angle and area distortion. Then all vertebrae are reconstructed using an adaptive resampling method based on the remeshing algorithm of Fuhrmann et al. (19). From this reconstructed training set, we build the SSM (Fig. 4) with the standard approach of Cootes et al. [14].

**2.5 Active Shape Model Segmentation**

The trained SSM is used in an ASM to accurately segment the vertebrae. For initialization...
tion, the learned mean vertebra is interactively placed into the image and then the automatic ASM segmentation is triggered. We use the standard ASM segmentation approach [14], which iteratively refines the segmentation. The algorithm terminates after a fixed number of 50 iterations.

The local appearance model of our ASM exploits that the boundaries of vertebrae usually have a strong gradient in CT images, and that the bone has considerably higher intensity than the background. Let $v$ be a candidate landmark position, $n_i$ be the surface normal of the landmark and let $(n_1, n_2, n_3)$ be an orthonormal basis. We sample the image gradient $G(v) = \langle G_1(v), G_2(v), G_3(v) \rangle$ at $v$ using finite differences, that is $G_i(v) = I(v + n_i) - I(v - n_i)$. The appearance of the image at position $v$ is assessed by the function $F(v) = \frac{1}{2} (-G_i(v)||G(v)|| + 1) \cdot ||G(v)||$. A high value of $F(v)$ means that the gradient at $v$ is strong, and that the image intensity in surface normal direction decreases.

Application of the ASM to several vertebrae in the image data sets results in a set of labeled vertebrae. These labeled voxels (▶Fig. 5) define the region where the BMD assessment is performed.

### 2.6 Spatial BMD Distribution and Bone Constitution

In their publication, Nickoloff et al. [9] obtain the values for $\chi^{low}$ and $\chi^{high}$ by computing the mean image intensity over the whole trabecular region of the vertebral body. Instead of this global mean computation, we do the averaging by computing a weighted intensity value for each voxel by a Gaussian smoothing of the image data.

This emphasizes the contribution of each single voxel with respect to its neighbors leading to the possibility to derive the spatial BMD distribution at pixel level. Then, we explicitly solve ▶Equations 1 and 2 for $V_{TB}$ and $V_F$ and derive the value for $V_T$. The BMD value $\rho_{BM}$ is solely dependent on the value of $V_{TB}$ and is given in $g/cm^3$ [9]:

$$\rho_{BM} = \frac{I \cdot V_{TB}}{1 + \lambda}$$

(3)

with $\lambda = 2.11$ and $l = 3.06$.

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### 2.7 The Barycentric Space of Fractional Volumes

Since the three fractional volumes $V_{TB}$, $V_F$, and $V_T$ are positive values and sum up to 1 they form a barycentric space: represented by a triangle where all points are defined by a unique combination of the three considered values (▶Fig. 6). The BMD computation step described above assigns to each considered voxel a 3-tuple $(V_{TB}, V_F, V_T)$. Thus, we have a representation of the trabecular bone composition of the small region covered by the voxel and its close vicinity. By mapping that 3-tuple to color the spatial distribution of the fractional volumes can be displayed giving an answer to the question: What is the composition of the trabecular bone?

### 2.8 Visualization

For the display of the computed values, we want to be able to examine the BMD as well as the bone composition of the trabecular bone and show the spatial relation to the other parts of the vertebra. Therefore, we generate two new image data sets $I_{BM}$ and $I_{comp}$ based on the input image data: For the voxels lying outside the region defined by
the mask, we simply copy the intensity values from the low energy image and shift them above 4095, i.e., \( I_{BDM,\,comp} = I_0 + 4096 \). The voxels inside the mask are set corresponding to the computed values for BMD and bone composition, respectively. Thus, in data set \( I_{BDM} \) the voxels contain the computed values \( \rho_{BM} \) in g/cm\(^3\) whereas the position in the barycentric space is determined by \( I_{comp} \). That way, the color transfer function can be defined to provide a standard gray level visualization for the unchanged voxel intensities above 4095 and a color mapping for values ranging from 0 to 4095.

Typical values for bone density have been investigated for a large patient cohort \[20\]. For the three types of vertebrae, there are different typical BMD value ranges (▶Table 1) and we base the color mapping on these measurements. Thus, depending on the type of vertebra the BMD values are mapped to color employing a perceptually based red-to-blue color map\(^4\). Here, low density regions appear reddish, areas of normal density white, and high density regions bluish (▶Fig. 10).

The computed bone composition is given as a 3-tuple \( (V_{TB}, V_F, V_T) \). We assign a qualitative color scheme to the large triangle’s corners: blue for \( V_{TB} \), yellow for \( V_F \), and brown for \( V_T \). The values inside the triangle are interpolated linearly. Thus we can map the computed 3-tuples to color. Similar approaches have been proposed for direct volume rendering of anisotropy measures derived from diffusion tensor image data \[21\]. Normally, there is no trabecular region containing only one single volume fraction \[9\], i.e., the corner regions of the outer triangle are never reached. In order to provide visualizations with strong color differences to better distinguish between different distributions of the fractional volumes, the base colors are also assigned to the inner triangle’s corners (▶Fig. 6).

Several 3D visualization methods are provided by our software. The clinician has the choice between a semi-transparent direct volume rendering (DVR), a minimum-intensity projection (MINIP) as well as a display of the volume data using three orthogonal slices.

### 2.9 Evaluation Methodology

The evaluation of our methods was two-fold. First, we used image data from 29 cadaveric vertebrae. They originated from three osteoporosis patients – one male as well as two females – representing thoracic, lumbar as well as cervical vertebrae. DECT image data (Siemens SOMATOM Definition) was acquired at 80 and 140 kV tube energy, respectively. The resolution of these data sets was 0.49 × 0.49 × 2 mm\(^3\). Second, we did a retrospective examination of DECT data from two real patients that had been acquired for other diagnostic reasons: pulmonary angiography and bone removal in whole body angiography, respectively. Therefore, it contained multiple thoracic and lumbar vertebrae, respectively. The tube peak energies were 100 and 140 kV for these data sets and their resolution was 0.62 × 0.62 × 0.5 mm\(^3\) and 0.62 × 0.62 × 0.7 mm\(^3\), respectively.

As a preprocessing step, the region of interest in the trabecular bone had to be delineated. For the cadaveric specimens, we employed the interactive deformation method which took between 2 and 4 minutes per vertebra. For the real patient data, our ASM approach was used which ran autonomously and provided the delineation of the vertebra in about 15 seconds per vertebra. For each of the latter data sets, three consecutive vertebrae were segmented this way (▶Fig. 5).

All subsequent BMD computations were performed automatically and restricted to the voxels covered by the mask image. The spatial density distribution was computed for all data – taking approxi-
For testing our hypothesis that DECT is better suited than the current gold standard DXA as an indicator for regional bone stability, we additionally used DXA data of the same cadaveric specimens. For this, a commercial device (DEXA Scan, Hologic) was used and the corresponding software provided areal density values for the vertebral bodies of the examined specimens. After data acquisition (DECT and DXA) for all vertebrae, pedicle screws (Biomet®, Omega®) were drilled through left and right pedicle and positioned horizontally with respect to the upper vertebral endplate. For all examined specimens, the left and afterward the right pedicle screw was pulled out – thereby at least partially destroying the vertebra. The forces necessary for that were measured by an Instron 8874 device (American Standards of Testing Machines) and stored. Due to the partial destruction of the vertebra after pulling out the left pedicle screw, we considered only the values for the left screw for the correlation examination.

3. Results

3.1 DECT/DXA vs. Force Measurements

For evaluating the correlation between DECT data and pull-out forces, the bowling pin template (Fig. 2) was used to delineate the region of the vertebra where the pedicle screw was placed afterward. We restricted our tests to the left pedicle screw due to the reasons given above. From the spatial density distribution, a global BMD value for that region was computed. Afterward, it was compared to the measured pull-out forces. Figure 8 shows the correlation between the computed BMD values and the force measurements. It can be seen that there is a strong linear relation – coefficient of determination $R^2 = 0.8242$ – between both sets of values.

In contrast to that, plotting the DXA values vs. the pull-out forces does not show such prominent correlation with a much lower coefficient of determination $R^2 = 0.4815$. Thus, our hypothesis stated above that DECT is more suited for measuring local bone stability than DXA is underpinned by our measurements.

3.2 Visualization

The visualization method using three orthogonal planes which can be interactively
moved through the image data set turned out to be an efficient tool for diagnosis. Especially the possibility to probe single voxel positions and get the corresponding BMD values displayed on the screen (Fig. 10) helped together with the color coding of the spatial BMD distribution to quickly examine the data sets.

A similar visualization was used for the display of the bone constitution. This novel information representing the fractional volumes provides additional knowledge about the trabecular bone – whether they are dominated by non-adipose tissue or fat (Fig. 10). This information could not be assessed so far and stands for added diagnostic value using our methods.

However, the orthopedist (K.K.) preferred the DVR method in the case that the BMD computation had been restricted to the region where a pedicle screw should be placed. The semi-transparent display of the data set (Fig. 11) allowed him to get an overview about the 3D relationships between the areas of different density.

In addition to the data stemming from cadaveric specimens we examined retrospectively two data sets from real patients. With our method we did find some smaller areas of severely lowered BMD values in one of the data sets. This example is shown in Figure 12 and contains noticeable areas of low BMD especially in the uppermost vertebra (L1). Again, the visualization using three orthogonal planes together with the direct probing was an efficient method for a detailed analysis of the computed BMD distribution.

4. Discussion

We have presented a comprehensive approach for the computation of quantitative measures related to BMD and trabecular bone composition in vertebrae and their visualization. To our knowledge, this is the first method relying on state-of-the-art DSCT imaging technology. The main contributions of our work that is based on Nickoloff’s method [9] are its extension to the computation of the spatial BMD distribution, the development of an automated method for vertebra segmentation using a single SSM, as well as the introduction of the barycentric space of fractional volumes.

We have hypothesized that DECT is better suited than the current gold standard DXA for the examination of local bone stability. Our quantitative evaluation clearly shows a strong linear correlation between regional BMD values computed with our method based on DECT. A comparison with derived DXA values representing the whole vertebral body reveals that the correlation for the latter is less prominent. The reason for that is two-fold. First, the trabecular bone in a vertebra is not a homogeneous region. Consequently, an averaging over the whole vertebral body will lead to a different bone density value than in the case where only a specific sub-region is considered. Second, DXA provides an areal density value that – due to the projective nature of the image acquisition – mixes density information for both, trabecular as well as cortical bone. Considering both known limitations of the current gold standard in osteoporosis assessment, 3D imaging techniques like DECT and also QCT have a clear advantage.

The possibility to easily interact with the displayed volumetric data is a prerequisite for an application in the clinical routine. Another requirement for data sets from real patients is the fast and automated delineation of the regions of interest, i.e., the vertebrae. Our novel ASM based segmentation approach is robust and has the unique feature that one single SSM is built which can be applied to different vertebrae – here L1 to L3 and Th10 to Th12. This distinguishes our method from others where a specific SSM is built for each vertebra type (e.g.,
The possibility to assess and display the bone composition gives new insight into the complex structure of vertebrae.

The clinical importance of this work is the possibility to replace DXA as the current standard imaging modality for bone density assessment. This would not mean to use yet another modality, but to have a set of new diagnostic tools. Another important aspect is the possibility to analyze DECT image data retrospectively. There are an increasing number of applications where such data sets are acquired in the clinical routine. Our method provides the opportunity to extract additional diagnostic information from those available data sets. As shown in one example above (Fig. 12), BMD can be assessed as a by-product from diagnostic scans systematically performed for other reasons such as oncologic stagings, trauma scans or preventive medical examinations.

However, those retrospective examinations also represent an ethical problem. Using our novel method there are signs for areas of low BMD in one case (Fig. 12). Does this justify an additional examination with the current gold standard method DXA? Can the clinician trust our DECT based computations? For now, our methods are evaluated only by force measurements on cadaveric specimens. Those experiments can certainly not be performed with real patients. Here, future work is necessary in order investigate the correlation between the spatial BMD distribution obtained with our method based on DECT data and QCT which also provides a 3D measurement of BMD.

5. Conclusions

DECT image data is gaining importance in radiological diagnosis. Assessing BMD is another application of this imaging technology. Compared to the current gold standard DXA it has the advantage that it represents 3D data providing volumetric information that can be used for the computation of the spatial BMD distribution as shown in this work. This is better suited for examining local bone stability than DXA. In contrast to QCT it has the advantage that no specific phantom has to be scanned together with the patient in order to be able to convert the image data to BMD values.

Our developments represent a comprehensive method for an in-depth analysis of the trabecular bone. This can also be done retrospectively on DECT data acquired for different diagnostic reasons. We expect an increasing usage of DECT image data in the radiological departments and thereby our work will hopefully make a contribution to a better patient care.

References

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