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Statistical Analysis of Sacral Bone Density using a CNN-based Atlas Creation on a Large-scale CT database

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Abstract

Fragility fracture of the sacrum has been an issue for elderly people. Research has been limited for the sacrum partly because its shape is complex with large inter-subject variation. Also, large-scale statistical analysis of its shape and density distribution has been limited mainly due to the computational load in establishment of the voxel correspondences, i.e., deformable registration.

In this study, we employed a convolutional neural network (CNN)-based deformable registration algorithm in the analysis of the sacral bone. The algorithm we employed, VoxelMorph (Dalca et al. Med Image Anal 2019), is characterized as an unsupervised algorithm where no ground truth deformation field is required. The algorithm also allows to create a conditional deformable template, which is a volume image exhibiting smallest deformation field from all samples with specific attributes (e.g., age, sex, etc.), which in short represents the "average" (or "centroid") image among the specific age and sex group. We applied it on a database consisting of 837 CTs (149 males, 688 females, 58.14 ± 14.73 y.o.) of the pelvis region, where the sacral bone was segmented and masked. We computed the templates corresponding to ages of 20 to 80 for male and female. The templates visually illustrated reduction of the bone density with aging in both male and female. The quantitative analysis showed that the average CT value over the sacrum region was reduced from 135.73 HU to 39.88 HU for 20 y.o. template to 80 y.o. template.

1 Introduction

With the advent of the aging society, fragility fracture of the sacrum has been an issue for the elderly people as it is often accompanied with pelvic ring injury and other vertebral fractures [1]. These fragility fractures occur in low energy trauma such as fall from standing, but is crucial as bed rest is likely required and subsequent loss in the activities of daily living is often found. Several previous studies reported the management and treatment method of sacral fractures [2,3]. However, majority of these previous reports are based on patients who are relatively young with the fracture occurring in a high energy trauma. Thus, there is still paucity of research in how fragility fracture of the sacrum should be evaluated and treated.

A previous study used statistical shape modelling and reported a relatively large variance in the shape of the sacrum [4]. Further, other recent studies reported the relationship between the HU of the spine and the sacrum [5, 6]. However, the number of subjects analyzed was small (less than 100 cases), limiting the analysis of age-related changes in the density distribution, which is expected to play an important role in the prevention of fragility fractures.

To this end, we propose an application of convolutional neural network (CNN)-based deformable registration algorithm called VoxelMorph [7, 8], allowing significantly fast deformable registration (i.e., establishment of voxel correspondences) as well as construction of atlas templates associated with specific attributes such as age and sex, in order to analyze the age and sex dependent changes in the shape and density of the sacral bone using a large-scale CT database.

2 Methods

Training of CNN-based deformable registration

CT images that were acquired for CT-based navigation hip surgery for 837 cases (149 males, 688 females, 58.1 ± 14.7 y.o.) were analyzed. The field of view was 360×360 mm2 and the matrix size was 512×512. The original slice intervals were 1.0 mm. We used the Bayesian U-Net [9] for segmentation of the sacrum region, cropped the volume with its bounding box, and replaced the voxels outside the sacrum with -1000 [HU]. The cropped volume was resampled to 160×160×160 with linear interpolation. In the learning phase, 737, 50, 50 CT images were used as training, validation, and test data.

We trained the VoxelMorph networks on a workstation with an Intel Xeon processor (2.8 GHz, 4 cores) and NVIDIA GeForce GTX 1080Ti. We used adaptive moment estimation (Adam) for 500 epochs at the learning rate of 0.0001. MSE was used as a loss function.

Generation of the conditional templates

The implementation of atlas generation by Dalca et al [8] was used. 837 sacrum volumes with the attribute of sex and age were used. Templates for the ages of 20 to 80 were generated.

Evaluation of the results

Digitally reconstructed radiographs (DRRs) in anterior-posterior direction was created by integrating HU value along the ray. Following the evaluation method in [5], we measured the average HU value along the transsacral corridors on the template. We manually selected a column shaped region with 7.0 mm diameter laterally at S1 region considering the transsacral implant. The mean HU value within each plane perpendicular to the column shape was calculated.

3 Results

Figure 1 shows the detail of our dataset samples and the average density over the sacrum region as a function of age. There were more than 75 samples in each age group through 40s to 70s for females and the mean intensity of the sacrum decreased as age increased.

Figure 2 shows the results of the learned sacrum atlas templates. The DRRs and the coronal slices clearly indicated the reduction of overall bone density. The analysis of sub-regions, which were derived from the deformation field between the unconditionally learned template and each sample, demonstrated the aging-related changes in local density. The difference of the Hounsfield Unit between the ages shows that older group have less value. However, the decrease rate should be different between the part in the slices.

4 Discussion

We have proposed and experimentally evaluated an application of CNN-based deformable registration and atlas creation in the analysis of the sacral bone using a large-scale CT database, which enabled detailed analysis of the HU values across the age and sex groups.

Previous methods used for creating atlases, such as Symmetric Normalization (SyN) [10], required a large amount of time for the registration, preventing the analysis with a large scale data set. For example, in [5, 6], less than 100 cases were analyzed for the atlas generation. Our results revealed that HU decreases for every age group in female (Fig. 1), and that the distribution of the HU is similar across the groups, resulting in a constant decrease in HU across the regions of the transsacral corridor (Fig. 2). However, the same tendency was not found for males. As the number of male patients included in this study was limited, analysis with a larger cohort is deemed necessary.

There are some limitations to this study. First, as majority of the cases were patients that underwent total hip arthroplasty (THA), selection bias may have affected the results. We are now planning further analysis with a larger dataset (>12,000 cases) including patients without hip diseases to solve this problem. In the second place, we have not yet validated the accuracy of the deep learning model with our dataset. For validation, we need to calculate the Target Registration Error (TRE) and compare it with existing methods. Another limitation is the absent of intensity calibration to convert Hounsfield units to volumetric bone mineral density (vBMD) for direct comparison across groups. CT datasets analyzed herein contain the image calibration phantom, however, converting HU to vBMD is yet to be performed. This is a component of our future analysis.

5 Conclusion

An approach for a large-scale statistical analysis of the shape and density of bones was proposed. The experiment using sacral bone demonstrated promising results which suggested a potential to be extended to the application in diagnosis, treatment planning, and drug development for osteoporosis in various anatomical regions.

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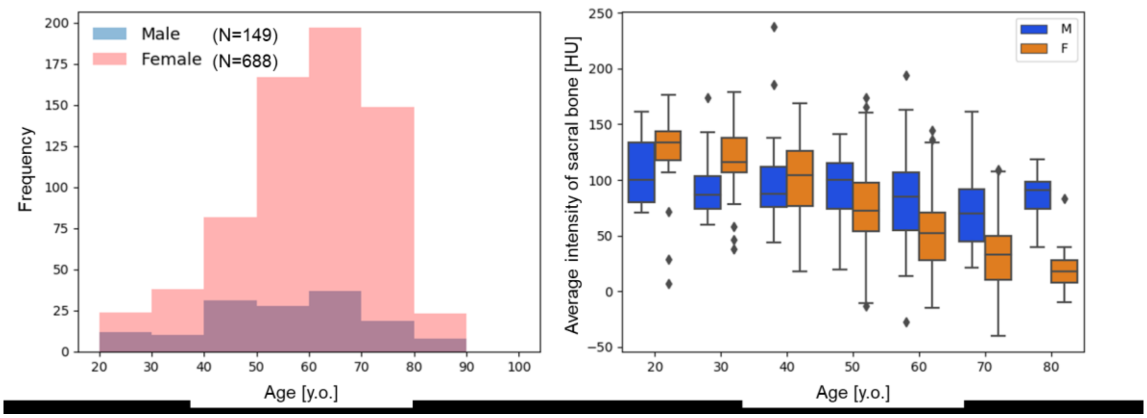

Figure 1: Demographic distribution and overall property of the sacral bone density. (Left) histogram of the sample population, (right) box and whisker plot of the average intensity of the sacral bone. 50s-70s were the most frequent samples in our database.

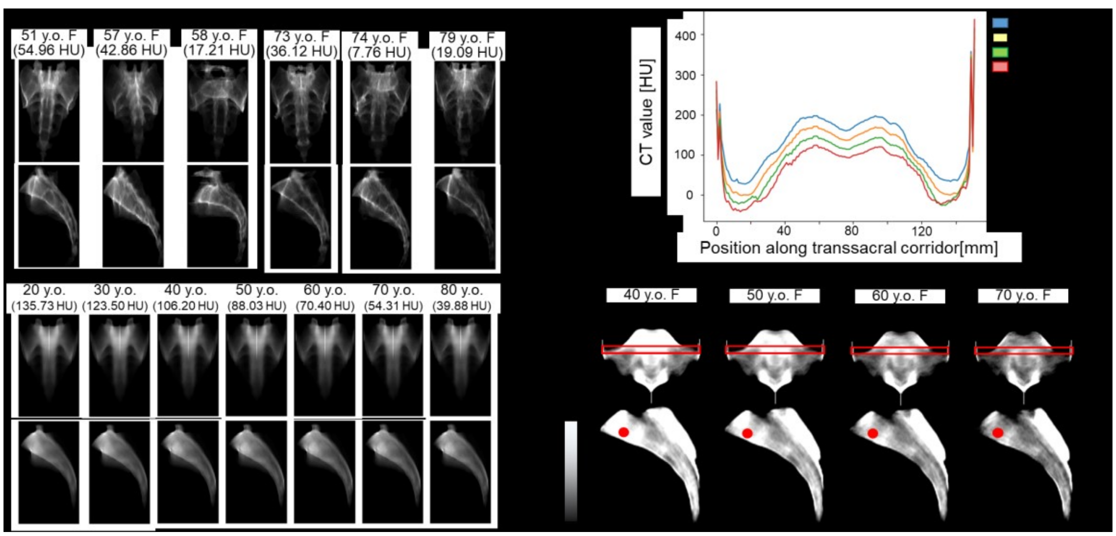

Figure 2: Results of learned sacrum atlas templates. The visualizations in (a) and (c) show digitally reconstructed radiographs (DRRs) in anterior-posterior direction (upper row) and coronal slices at the middle of the sacral bone (bottom row). (a) atlas template and two randomly selected samples from 50s and 70s. (b) The transition of the average intensity on the transsacral corridor from ages 40 to 70. The intensity is decreasing as they get older. (c) Female atlas templates for ages 20 to 80, illustrating, for example, reduction of the bone density. (d) Horizontal and sagittal cross sections for ages 40 to 70. The red rectangles and circles show the area of the transsacral corridor. The shading is darker as the age of the atlas older. It follows the result shown on (c).