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Aging calvaria: Introduction of a numerical method to improve information extraction from computed tomography images

Martin Obert[a,*], Laura Rodenheber[a], Marian Kampschulte[a], Gabriele A. Krombach[a], Marcel A. Verhoff[b]

[a] Department of Radiology, University Hospital Giessen, Justus-Liebig-University Giessen, Klinikstrasse 33, D-35392 Giessen, Germany
[b] Department of Forensic Medicine, University Hospital Frankfurt, Goethe University, Kennedyallee 97a, D-60596 Frankfurt/Main, Germany

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ABSTRACT

Objectives: This study explored whether age-relevant information may be hidden in density histograms of computed tomography (CT) images of calvaria and whether this information can be extracted by a novel “histogram's functional shape” (HFS) analysis method. The method was compared with other CT-based bone analysis methods.

Materials and Methods: Software was written that reanalyzed flat-panel CT data from European human skulls (120 female; 221 male). Calvarial data were segmented from these CT images and density histograms were produced thereof. A nonlinear curve fit was then used to calculate the HFS method. Seventeen multinomial logistic regression (MLR) model calculations were performed in a competition calculation in which the results of the HFS method, and other radiologically defined bone image markers were used as covariates to predict age-at-death (AAD). Age predictions for individual skulls were calculated for five equidistant age groups ranging from 0 to 100 years.

Results and Conclusions: The HFS method could be applied successfully. Chi^2_{HFS} was «0.05 in all 675 skull density histogram analyses. When MLR model calculations that use covariates from one method only were compared, the HFS method had a higher AAD prediction power. The overall ranking list is led by the models that used multiple covariates from different methods: The best correct group assignment was 62.5% (Nagelkerke's pseudo R^2 (NR^2) =0.76) for females, and 51.6% (NR^2=0.43) for males. Hence, a novel image marker was introduced, and it was shown that the use of combined methods is superior to individual methods.

1. Introduction

Age-at-death (AAD) estimation is a basic issue in forensic medicine for the identification of unknown bodies, and many studies have been devoted to this topic [1–35]. Currently, no satisfactory, general methods exist that enable an accurate age estimation of individuals. Within this background, this study is a continuation of a larger project devoted to the improvement of age-estimation methods based on quantitative analyses of computed tomography (CT) images in forensic medicine. Such quantitative methods, which are also called biomarkers, are based on objective, well-defined numerical image analysis methods. Numerical image analysis has the advantage of operating without the inherent inconsistencies related to subjective human visual image inspections. Furthermore, quantitative analyses are easier to reproduce than visual inspections. In earlier studies, a calvarial database collection was set up using data acquired with a high resolution flat-panel CT system, the eXplore Locus Ultra (eLU). In two studies the skull-bone density was examined [33,34], based on the attenuation of x-rays in the CT acquisition. In a third examination [35] the fractal dimension, (F), was evaluated as a measure with which to estimate the geometrical irregularity of the trabecular skull-bone structure. These bone density and fractal studies disclosed that there is a sex difference between female and male skulls: While a weak correlation between “age” and “bone density,” (D), and between “age” and “fractal dimension” was found for female calvaria, no such correlation was found for male calvaria. Thus, the found correlations were without practical relevancy for AAD estimates, because the data were too strongly scattered.

In this study, we postulated that age-relevant information is encoded in the complex shape of Hounsfield unit distributions in CT

* Corresponding author.
E-mail address: martin.obert@radiol.med.uni-giessen.de (M. Obert).

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images of calvaria. Hounsfield units (HU) are the gray-level values in CT images, and the frequency of HU as a function of HU is synonymously called “HU distribution,” “density curve,” or “density histogram.”

To test this hypothesis, we specifically developed a numerical bone analysis procedure with which to extract this age-relevant information. The procedure entailes several steps: First, histograms from CT images of segmented calvaria are generated. Next, these histograms are transformed such that a nonlinear curve fit algorithm can be used to characterize transformed histograms by fit parameters. Because this combination of numerical steps describes the histogram's functional shape, it is called “HFS”. To study the numerical robustness of the HFS approach, fit parameters and quality-of-fit statistics were evaluated for each of the calvaria from the 341 subjects in our previously established skull database. Numerical robustness is a precondition that must be fulfilled prior to the study to assess whether the HFS method can be meaningfully applied in AAD estimations or not. To study the age prediction accuracy of the HFS method, the individuals of known age were grouped into five age groups, each of 20 years width, ranging from 0 to 100 years. Afterwards, a multinomial logistic regression (MLR) model, in which the covariates of the MLR were based on HFS fit parameters, was used to calculate the classification predictions for the different age groups.

To find out whether it is reasonable to introduce a new numerical AAD concept for the analysis of CT images, it was necessary to compare the new method with existing methods and to perform a quality ranking of the different methods. At best, the new HFS method outperforms existing methods. For this purpose, the classification properties of the HFS method were compared with other CT image based AAD prediction methods, for example the radiological bone density (D), fractal dimension (F), mean value (MV), variance (V), skewness (S), and kurtosis (K). Seventeen different MLR model calculations using the individual, named parameters, as well as combinations thereof, were evaluated as covariates in the MLR. MV, V, S, and K are additional quantitative image features, based on the statistical moment analysis of density histograms, which were also estimated. Calculations were performed separately for female, and male, frontal and occipital calvaria. Results were compared on the basis of their ranking performance in a MLR model competition.

2. Materials and Methods

This study was approved by the Ethics Committee of the Faculty of Medicine, University of Giessen, Germany, and was a cooperative effort between the Department of Forensic Medicine and the Department of Radiology. For the study, we used an existing calvarial database collection, already used in earlier studies [32,33,35], that had been generated as follows: Radiological examinations were performed on 341 human skulls (120 female; 221 male) of European ancestry from cadavers of known age. All calvaria were excised during regular autopsies and later returned to the body after being carefully cleaned and radiologically investigated. Fig. 1 shows the photograph of an excised calvarium positioned on the specimen holder of the CT scanner. Scanning was performed using the eXplore Locus Ultra, an experimental volumetric micro-computed tomography system, manufactured in 2006 by GE Healthcare, London, Ontario, Canada. The special feature of this CT system is a flat-panel radiation detector. One thousand views were taken during one gantry rotation of 16 s acquisition time at 140 kVp and 10 mA. The field of view (FOV) of the scanner was 151.04×151.04×100.30 $(mm)^3$ in the x-, y-, and z-direction, where the z-direction follows the CT-table direction (see arrow in Fig. 1) and corresponds to the anterior-to-posterior direction of a skull. The system's limited FOV of 100.30 mm in the z-direction necessitated the acquisition of two separate “half-scans” for the frontal and occipital regions of the same calvarium, instead of one complete scan, see Fig. 2. Data were reconstructed into a 512×512×340 voxel matrix using a cone-beam filtered back-projection algorithm. The same scanning protocols and image reconstruction software was used for all scans. Calvarial half-scans of 117 female frontal bones, 120 female occipital bones, 217 male frontal bones, and 221 male occipital bones were taken. Scanner malfunctions were the reason why, in some cases, only one half-scan could be obtained for some of the calvaria. This explains the discrepancy in the number of acquired frontal and occipital bone scans. In total, 675 half-scans were acquired. The subjects’ ages were calculated to an accuracy of one day, as the difference between “date of investigation” and “date of birth.” At the bottom, Tables 1–4 show the frequency distributions for frontal and occipital bones for both sexes.

Fig. 1. Photograph of the eXplore Locus Ultra CT scanner. The inset image shows an excised calvarium positioned on a sponge on the scanner's specimen holder.

2.1. Calvarial segmentation and definition of “density histograms”

The segmentation of the calvaria ensured that only relevant voxels of a CT dataset were considered in the subsequent numerical analysis and that other objects, such as the specimen holder of the CT-table, were removed, see Fig. 3. The segmentation was carried out by a bone threshold operation in which all voxels with a Hounsfield unit (HU) value of less than 100 were excluded from the CT image. This segmentation was feasible, because only voxels with values larger than 100 HU belong to bone. Because the specimen holder or air have much lower HU values, they were, hence, eliminated. Next, a histogram consisting of the frequency of a given HU as function of HU was calculated from the segmented bone voxels. Using the image analysis software IDL®, Version 8.4, Exelis Visual Information Solutions, Boulder, CO, USA, an in-house computer program was developed that read in the CT data from the subjects, performed the bone segmentations, and calculated the density histograms. Examples of density histograms are shown in Fig. 4.

2.2. Histogram's functional shape method

First, the density histograms were transformed into cumulative histograms. Next, the cumulative frequencies of the histograms were normalized to 1. These calculations define a normalized cumulative histogram with values in the range from 0 to 1 on the frequency-axis, in this case, the y-axis. In later line graphs, this axis is labeled “normalized frequency”. The original HU-scale, on the x-axis, of the density histograms ranged from 100 HU up to the maximum HU value present