

The radiological diagnosis of fenestral otosclerosis: the utility of histogram analysis using multidetector row CT

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Received: 25 November 2013 / Accepted: 4 February 2014 / Published online: 18 February 2014
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Abstract Bone density measurements using high-resolution CT have been reported to be useful to diagnose fenestral otosclerosis. However, small region of interest (ROI) chosen by less-experienced radiologists may result in false-negative findings. Semi-automatic analysis such as CT histogram analysis may offer improved assessment. The aim of this study was to evaluate the utility of CT histogram analysis in diagnosing fenestral otosclerosis. Temporal bone CT of consecutive patients with otosclerosis and normal controls was retrospectively analyzed. The control group consisted of the normal-hearing contralateral ears of patients with otitis media, cholesteatoma, trauma, facial nerve palsy, or tinnitus. All CT images were obtained using a 64-detector-row CT scanner with 0.5-mm collimation. AROI encompassing 10×10 pixels was placed in the bony labyrinth located anterior to the oval window. The mean CT value, variance and entropy were compared between otosclerosis patients and normal controls using Student's *t* test. The number of pixels below mean minus SD in the control ($\%Low_{cont}$) and total subjects ($\%Low_{total}$) were also

compared. In addition, the area under the receiver operating characteristic curves (AUC) value for the discrimination between otosclerosis patients and normal controls was calculated. 51 temporal bones of 38 patients with otosclerosis and 30 temporal bones of 30 control subjects were included. The mean CT value was significantly lower in otosclerosis cases than in normal controls ($p < 0.01$). In addition, variance, entropy, $\%Low_{cont}$ and $\%Low_{total}$ were significantly higher in otosclerosis cases than in normal controls ($p < 0.01$, respectively). The AUC values for the mean CT value, $\%Low_{cont}$ and $\%Low_{total}$ were 0.751, 0.760 and 0.765, respectively. In conclusion, our results demonstrated that histogram analysis of CT image may be of clinical value in diagnosing otosclerosis.

Keywords CT · Otosclerosis · Histogram analysis

Introduction

Otosclerosis is characterized by pathological remodeling process of otic capsule [1–4] and one of the most common causes of hearing loss in adult patients. The etiology of the disease remains unclear. The diagnosis is made on the basis of patient's symptoms, family history, and normal tympanic membrane on otoscopic examination, audiometric evaluation, and radiological findings. High-resolution computed tomography (HRCT) is clinically useful to detect low-density lesions and excluding differential diagnoses such as ossicular chain dislocation. The low-density lesions are observed in active otospongiosis and otosclerosis [5–13]. The main otosclerotic focus is located in the ante fenestral region, which is the last area of endochondral bone formation in the labyrinth. Bone densities can also be measured in Hounsfield units (HU) by the accurate regions of

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interest (ROIs) setting [7–9]. However, small ROI choice may provide inaccurate diagnosis particularly in cases of otosclerotic foci confined to small area. Semi-automatic analysis with a larger ROI which nearly fills the ante fenestral region should be chosen for precise assessment. CT histogram analysis is designed based on an observer-independent method, and it has been reported to be useful in the diagnosis of various diseases [14–16]. Histogram provides the distribution of the CT value for all pixels in the ROI. Histogram analysis allows measurements of various parameters based on histogram shape as well as mean CT value.

Therefore, our purpose was to evaluate the utility of CT histogram analysis in diagnosing otosclerosis.

Materials and methods

This study was approved by the Institutional Review Board of our university hospital. 51 temporal bones of 38 patients with surgically proven otosclerosis (M:F = 6:32; mean age \pm SD: 49.0 \pm 12.4 years) and 30 temporal bones of 30 control subjects (M:F = 4:26; mean age \pm SD: 44.0 \pm 16.2 years) were included. The otosclerosis patients underwent temporal bone CT scan at our hospital between January 2008 and December 2012. The control group was consisted of the normal-hearing contralateral ears of patients with otitis media, cholesteatoma, trauma, facial nerve palsy, or tinnitus. Table 1 provides the clinical data of all subjects.

CT scan of the temporal bone

All CT images were obtained using a 64-detector-row CT scanner (Aquilion, Toshiba Medical Systems Corporation, Tokyo, Japan) with 0.5-mm collimation and a 512 \times 512 matrix. Transverse scans were acquired in a plane parallel to the orbitomeatal plane in the helical mode with 120 kV, 250 mAs, 1 second rotation time, 0.5-mm section thickness and overlap 0.3 mm with its adjacent slice, beam pitch 0.625, scan field of view (FOV) 240 mm, and display FOV

80 mm. All images were displayed at a window center of 400 HU and a window width of 4,000 HU on picture archiving and communication systems (Synapse, Fujifilm medical systems, Tokyo, Japan).

Inner ear measurements

A ROI encompassing 10 \times 10 pixels was placed in the bony labyrinth located anterior to oval window (Fig. 1) by one author (KY) using Image-J software (Version 1.45s, National Institutes of Health, Bethesda, MD, USA). The size of ROI was empirically determined to closely fit the ante fenestral region of the bony labyrinth. The pixels in each ROI were processed with histogram analysis. The mean CT value, variance, number of pixels below mean minus an SD in the control (%Low_{cont}) and total subjects (%Low_{total}) were measured for each ROI. %Low_{cont} and %Low_{total} represent the percentage of pixels with relatively low CT value. In addition, we calculated the entropy for each ROI, which is a parameter derived from the texture analysis. Entropy is one of the texture analysis parameters, and it is known to measure parametric inhomogeneity within the ROI [17, 18].

Audiometry

Each patient underwent an audiometric test in a double-walled sound room within 1 month before or after the CT examination. Air conduction, bone conduction, and the air–bone gap threshold were recorded at 250, 500, 1,000, 2,000, 4,000, and 8,000 Hz. The hearing levels for air

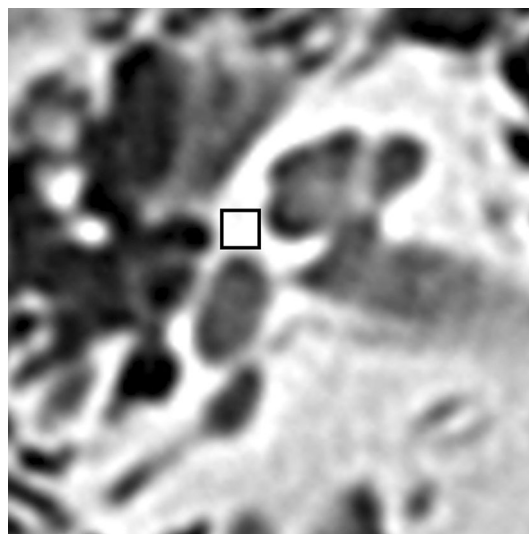


Fig. 1 Example of ROI placement. A ROI encompassing 10 \times 10 pixels was placed in the bony labyrinth located anterior to oval window

Table 1 Summary of clinical data

	Fenestral otosclerosis	Normal subjects
Cases	38	30
Ears	51 ^a	30
M:F	6:32	4:26
Mean age \pm SD (years)	49.0 \pm 12.4	44.0 \pm 16.2
PTA (range)	55.1 \pm 16.8 (32.5–105 dB)	8.3 \pm 4.5 (1.3–18.8 dB)

PTA pure-tone average

^a Thirteen patients had bilateral otosclerosis

conduction and bone conduction were calculated using the formula $(500 \text{ Hz} + 2 \times 1,000 \text{ Hz} + 2,000 \text{ Hz})/4$.

Statistical analysis

The mean CT value, variance, %Low_{cont}, %Low_{total} and entropy were compared between otosclerosis patients and normal ears using Student's *t* test. A *p* value of less than 0.05 was considered to be of significant difference. In addition, the area under the receiver operating characteristic curves (AUC) value for the discrimination between otosclerosis patients and normal ears was calculated. Pearson correlation coefficients were also calculated to determine whether there is a significant correlation between the mean

CT value and hearing level in the otosclerosis patients. All statistical analyses were performed using JMP 9 software (SAS Institute, Cary, NC).

Results

Figure 2 shows plots of mean CT value, variance, %Low_{cont}, %Low_{total}, and entropy. The mean CT value (Fig. 2a) was significantly lower in otosclerosis cases (mean ± SD = 2,005 ± 518 HU) than in normal ears (mean ± SD = 2,400 ± 149 HU) (*p* < 0.01). In addition, variance (Fig. 2b), %Low_{cont} (Fig. 2c), %Low_{total} (Fig. 2d), and entropy (Fig. 2e) were significantly higher

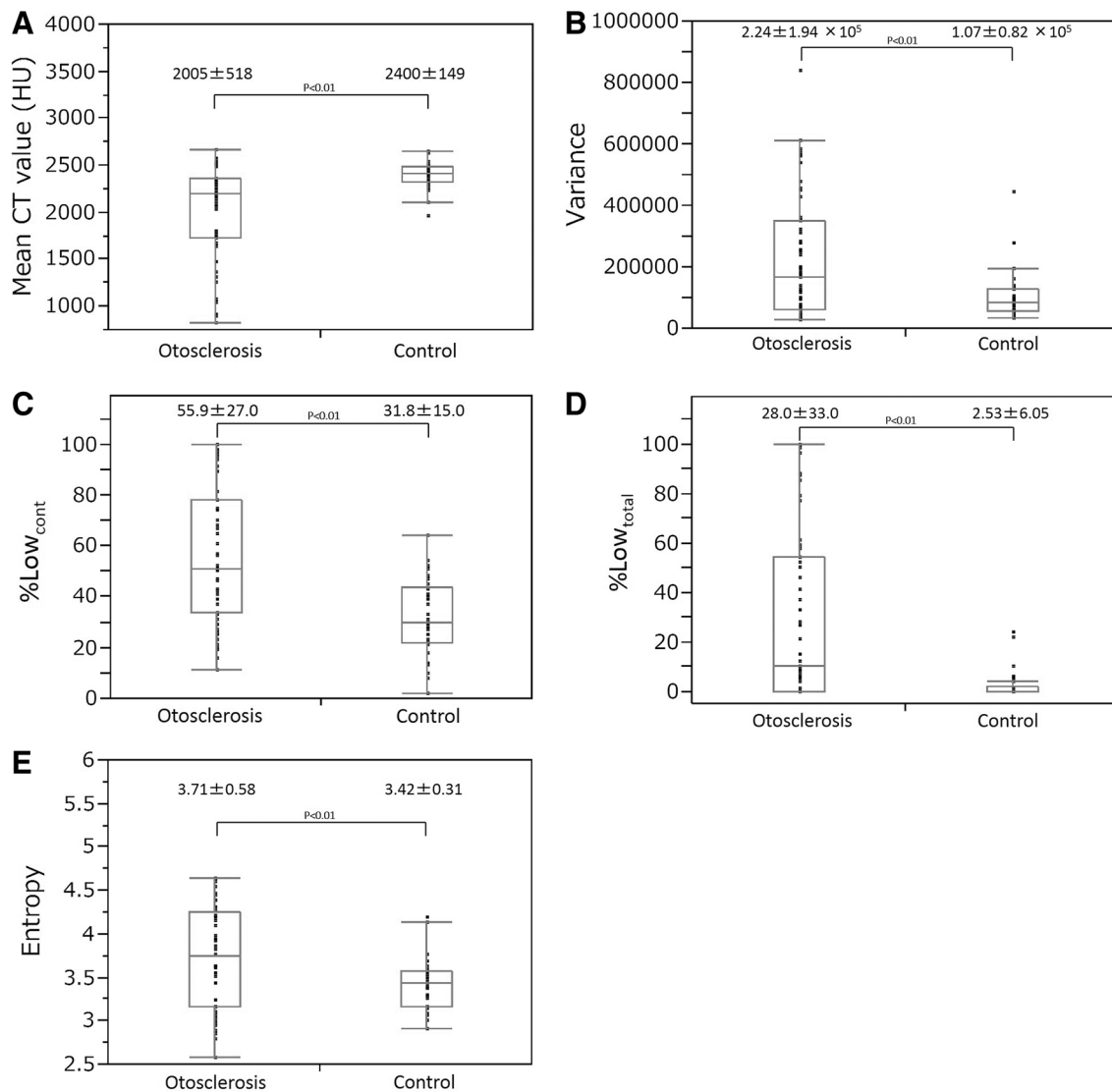


Fig. 2 Plots of mean CT value (a), variance (b), %Low_{cont} (c), %Low_{total} (d), and entropy (e) in otosclerosis patients and normal ears. The mean CT value is significantly lower in otosclerosis cases

than normal ears (*p* < 0.01). In addition, variance, %Low_{cont}, %Low_{total}, and entropy are significantly higher in otosclerosis cases than normal ears (*p* < 0.01, respectively)

in otosclerosis cases (mean \pm SD = $2.24 \pm 1.94 \times 10^5$, 55.9 ± 27.0 , 28.0 ± 33.0 , 3.71 ± 0.58 , respectively) than normal ears (mean \pm SD = $1.07 \pm 0.82 \times 10^5$, 31.8 ± 15.0 , 2.53 ± 6.05 , 3.42 ± 0.31 , respectively) ($p < 0.01$, respectively). The AUC values for the mean CT value, variance, %Low_{cont}, %Low_{total}, and entropy were 0.751, 0.666, 0.760, 0.765, and 0.658, respectively. No significant difference in AUC values was found among the five measurements.

Figure 3 shows the ROC curves for the mean CT value, %Low_{cont} and %Low_{total}.

Figure 4 demonstrates that no significant correlation was found between the mean CT value and hearing level in the otosclerosis patients ($\gamma = -0.14$, $p = 0.35$).

Figure 5 shows an example of otosclerosis cases.

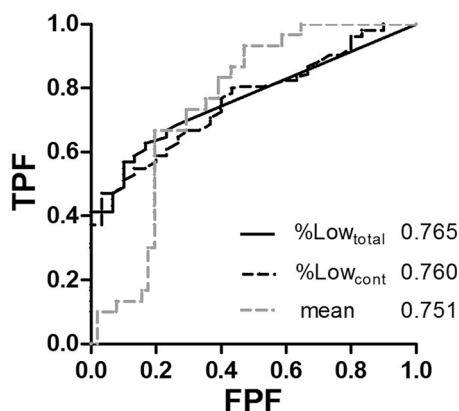


Fig. 3 The ROC curves for the discrimination between otosclerosis patients and normal ears by mean CT value, %Low_{cont} and %Low_{total}. TPF true positive fraction, FPF false positive fraction

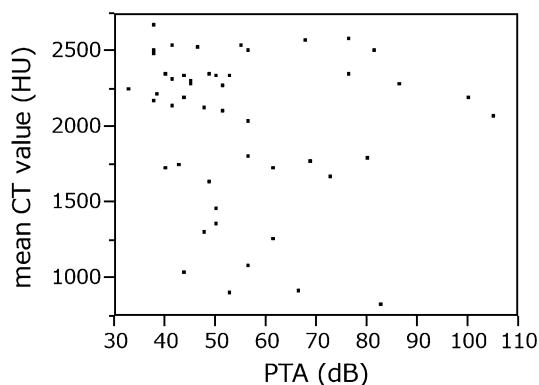


Fig. 4 The scatter plots between the mean CT value and hearing level in the otosclerosis patients. No significant correlation was found ($\gamma = -0.14$, $p = 0.35$)

Discussion

CT is the standard diagnostic imaging modality for detecting otosclerotic foci which offers the best spatial resolution. Bone density measurements using HRCT have been reported to be useful to differentiate between otosclerosis patients and normal ears [7–9]. In previous quantitative CT studies, small circular ROIs of 1 mm^2 were placed in the bony labyrinth [7, 8]. From a practical point of view, use of such a small ROI can be subjected to operator dependent biases. Histogram analysis based on measurement with larger ROI as used in this study should be a more reliable and reproducible method, although comparative study between the two methods is needed to confirm. As shown in Fig. 1, a ROI encompassing 10×10 pixels nearly fills the ante fenestral region in most cases, ensuring the reproducible ROI placement. Our results demonstrated that the mean CT value was significantly lower in otosclerosis patients than in normal ears (Fig. 2a), which is in line with the previous reports [7–9]. Notably, unlike the previous studies surgical confirmation was obtained in all cases in this study. Furthermore, our results indicated that this principle was also valid in the 13 patients with bilateral lesions.

In addition, we found that both %Low_{cont} and %Low_{total} were significantly higher in otosclerosis patients than normal ears (Fig. 2c, d). It is well known that the raw CT values can vary depending on the imaging parameters and conditions of image reconstruction [19]. The %Low_{cont} and %Low_{total} are independent from the mean CT value, and thereby less susceptible to the variations in raw CT values. These histogram-derived indices may be helpful in clinical setting where images from different scanners have to be compared.

Our results showed that the entropy was significantly higher in otosclerosis cases than in normal ears (Fig. 2e), which may correspond to pathological remodeling process of otic capsule in otosclerosis. The AUC value of entropy was lower than that of the mean CT value. We speculate that lower discriminating performance of the entropy might be due to inadequately small number of pixels to analyze the texture factor.

No significant correlation was found between the mean CT value and hearing level in the otosclerosis patients. Although some authors have found significant relationship between CT findings and the degree of sensorineural hearing loss [20, 21], Nelson et al. stated that even when extensive endosteal involvement with otosclerosis is present, hearing may remain normal, and the cochlear elements may remain predominantly normal in their histopathologic study [22]. The focus may include a number of components, such as bone formation by osteoblasts, bone destruction by osteoclasts, vascular proliferation, fibroblasts, and histiocytes. Moreover, otosclerotic and otospongiotic lesions can occur simultaneously, and

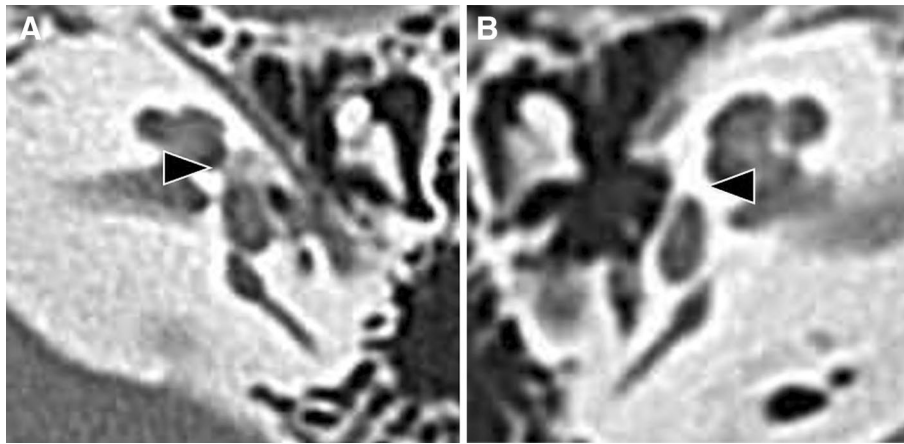


Fig. 5 a HRCT of a 50-year-old female with otosclerosis. A hypodense lesion is seen in the left fissula ante fenestram (*arrowhead*). Low mean CT value (1,259 HU), high %Low_{cont} (97) and %Low_{total} (77) are demonstrated in the ROI. **b** HRCT of a 31-year-

old female with normal hearing level (3.8 dB). No hypodense lesion is detected in the right fissula ante fenestram (*arrowhead*). The mean CT value (2,482 HU), %Low_{cont} (21) and %Low_{total} (0) in the ROI indicate typically normal pattern

one does not necessarily precede the other [4, 23]. Such complexity in the pathological process may account for the lack of correlation between mean CT value and hearing level.

Previous reports have shown that no otosclerotic focus was detected in 11–35 % of HRCT in clinically or surgically diagnosed otosclerosis patients [5–7, 9, 11]. Tringali et al. stated that it was impossible to differentiate between temporal bones with otosclerosis that had a normal-appearing CT scan and control group [9]. This situation was encountered in 19.6 % of our patients under the condition of an optimal cut-off value 2,366 HU determined by the ROC analysis of the mean CT value. This is the potential limitation of CT study.

In conclusion, our results suggested that histogram analysis of CT image may be of clinical value in diagnosing otosclerosis.

Conflict of interest The authors have no conflict of interest to declare.

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