

Histopathological differences in bony destruction of malleus and incus following mastoidectomy

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Abstract

Objectives: Upon direct inspection of surgically removed ossicles from the ears of patients with long-term post-mastoidectomy cavity problems, the extent of malleus destruction often appears greater in patients with a longer duration of cavity problems, whereas the extent of incus destruction does not appear to correlate with the duration of cavity problems. This study aimed to investigate this impression.

Materials and methods: As a result of total middle-ear reconstruction, 41 ossicles (21 malleus and 20 incus bones) were obtained from 31 patients with post-mastoidectomy cavity problems. The ossicles were examined histopathologically, and the proportion of lamellar bone area to total bone area (expressed as percentage lamellar bone) was measured. We also calculated the inter-operation time, i.e. the time period between the previous mastoidectomy and the recent total middle-ear reconstruction; this parameter was used as an approximate measure of the duration of the patient's cavity problem. Correlations between percentage lamellar bone and inter-operation time were calculated for the two ossicles.

Results: The range of inter-operation times was seven to 65 years. We observed a correlation between percentage lamellar bone and inter-operation time for malleus bones ($r = -0.512$, $p < 0.05$), but not for incus bones.

Conclusion: These results were in agreement with our pre-study impressions.

Key words: Mastoid; Chronic Otitis Media; Incus; Malleus; Otological Surgical Procedures

Introduction

Chronic ear infection with purulent discharge is often seen in patients who have previously undergone radical or modified mastoidectomy. This state is often referred to as a 'cavity problem'.

Total middle-ear reconstruction is indicated for such patients, mainly to improve the cavity problem and the coexisting hearing loss.¹ In the otolaryngology department of the University of Tokyo, total middle-ear reconstruction has been performed in many patients with cavity problems since 1993.²

We have previously described in detail the operative procedure for total middle-ear reconstruction.^{2–5} In short, a typical total middle-ear reconstruction procedure involves the following steps. (1) The infected skin and epithelium covering the open cavity are peeled off from the post-mastoidectomy cavity, and necrotic and granulation tissue removed. (2) The posterior canal wall and/or scutum are reconstructed using autologous cartilage or cortical bone. (3) The tympanic membrane is reconstructed using a temporal fascia graft. (4) The ossicular chain is reconstructed as in a type III or IV tympanoplasty.

During total middle-ear reconstruction, the ossicles are occasionally removed and submitted for routine pathological analysis to estimate the extent of bone damage. Most such ossicles are observed to be deformed, if not destroyed, by long-term cavity problems present for many years (sometimes several decades).

Macroscopic evaluation of such ossicles during and after total middle-ear reconstruction reveals variability in the degree of bone destruction present in the malleus and the incus. Malleus bones from patients whose mastoidectomy was performed long ago appear more severely damaged, compared with those from patients whose mastoidectomy was relatively recent, judging from the degree of deformity and roughness of the bone contour. On the other hand, the extent of damage affecting incus bones appears to vary randomly, independent of how recently the patient has undergone mastoidectomy. Findings from microscopic examination of ossicles are in agreement with macroscopic findings.

As a result of these clinical observations, we hypothesised that, in this clinical context, the

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process of bone destruction differed between the malleus and the incus.

To test this hypothesis, we conducted the present, retrospective study in order (1) to analyse quantitatively the degree of malleus and incus bone damage, and (2) to attempt to correlate these findings with the time elapsed between the patient's previous mastoidectomy and their recent total middle-ear reconstruction (defined as the inter-operation time; see below). In order to quantify the degree of bone damage, we determined (from histological sections) the proportion of lamellar bone area (lamellar bone representing normal, healthy bone tissue) to total bone area, expressed as percentage lamellar bone (see below). Chronic inflammation over many years results in destruction of lamellar bone, but the contour of the bone is mostly maintained by newly formed osseous tissue that replaces the defect. This regenerated bone is termed woven bone, immature bone or fibre bone.⁶ Woven bone is not seen in normal, healthy bone, and its presence always reflects a disease process.⁶

Materials and methods

Total middle-ear reconstruction has been performed in the otolaryngology department of the University of Tokyo since 1993. All ears surgically treated by total middle-ear reconstruction presented with cavity problems secondary to previous mastoidectomy. Of these cases, ossicles were obtained from 31 ears of 31 patients and were examined histopathologically. Both the malleus and the incus were harvested from 10 ears, the malleus alone from 11 ears, and the incus alone from 10 ears. Overall, 41 ossicles (21 malleus and 20 incus bones) were obtained.

Stapes bones were not evaluated in the present study.

Histological sections of malleus and incus bones from two normal ears, without ear disease, were included as controls.

The ossicles were fixed in 10 per cent formalin solution, decalcified in 5 per cent trichloroacetic acid solution, dehydrated in graded solutions of alcohol, and embedded in celloidin. Bone sections were stained with haematoxylin and eosin, mounted on glass slides and observed under a light microscope.

Only one section was selected from each ossicle for examination. Selection was based on a routine procedure followed within the pathology department of the University of Tokyo: the selected section was subjectively estimated to encompass the widest surface area, thus optimally representing the entire ossicle.

The selected section was photographed digitally and this image file stored on a computer. In most cases, a considerable portion of the bone tissue had been replaced by woven bone, and the proportion of lamellar bone was substantially decreased, compared with normal ossicles. Using a computer mouse, for each ossicle we manually outlined the area of lamellar bone that had escaped destruction by chronic inflammation, and calculated its ratio relative to the total bone area, using the National Institutes of Health image analysis software (Image

J; available from <http://rsb.info.nih.gov/ij/>). This ratio was termed the percentage lamellar bone. Thus, a small percentage lamellar bone was presumed to reflect severe inflammation of the ear, since a longer history of inflammation is associated with more extensive destruction of the bone. The total bone area was defined as the area within the bone contour, including lamellar bone and woven bone but excluding the bone marrow area. Newly formed cartilage tissue was included in the total bone area calculation, because it was regarded as having replaced defective bone tissue. The total bone area was also taken to include Haversian canals, small vessels and bone cavities containing osteocytes, because these structures are very numerous and are small enough to be neglected. Some specimens contained bone defects caused by technical procedures. These artefacts were excluded from the total bone area calculation. The distinction between lamellar bone and woven bone was generally straightforward, because the latter stained weakly with haematoxylin and eosin and contained more osteocytes. However, in some areas this distinction was difficult, because of ambiguous findings such as woven bone with recovery of lamellar pattern long after its formation. In the case of such obscure and relatively infrequent findings, the distinction was discussed and consensus was reached between the two examiners (TS and NY).

We defined inter-operation time as the number of years between the patient's first mastoidectomy (regardless of any other ear surgery performed subsequently) and their total middle-ear reconstruction during which ossicles were obtained. The inter-operation time represented a rough estimate of the duration of the patient's cavity problems. The inter-operation time was obtained from the patient's clinical history, obtained from the medical records. The timing of the first mastoidectomy generally depended on the patient's memory, and was usually described in such phrases as '38 years ago' or 'when I was 22 years old'. Inter-operation times were expressed as whole numbers of years. Inter-operation times of less than one year could not be evaluated accurately for all patients.

We analysed the correlation between percentage lamellar bone and inter-operation time, for malleus and incus bones separately, using linear regression analysis.

Results and analysis

Figure 1 shows a high-power photomicrograph of an incus section, showing lamellar bone, woven bone, bone marrow, ectopic cartilage tissue and an artefact. This figure provides an example of how the above components were distinguished from each other.

In the specimens studied, the percentage lamellar bone ranged from 0.3 to 70.4 per cent, and the inter-operation time ranged from seven to 65 years. In the two normal ears, the percentage lamellar bone was 100 per cent for both malleus and incus bones, as expected.

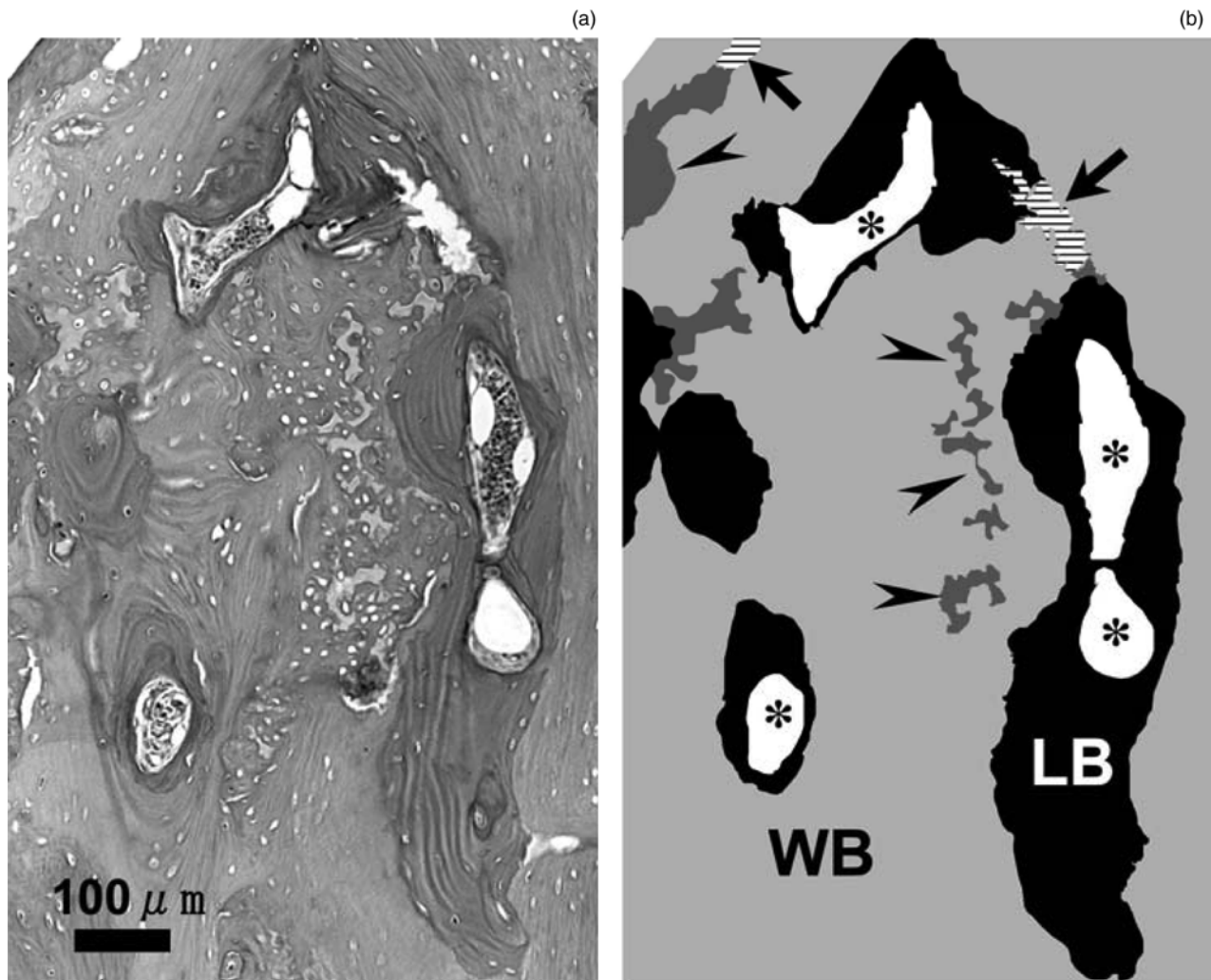


FIG. 1

(a) Photomicrograph of representative section (H&E). (b) Computerised image of (a); note lamellar bone (LB; black), woven bone (WB; grey), bone marrow space (asterisk; white), ectopic cartilage tissue (arrowheads; dark grey) and artefact (arrow; line pattern). This patient had undergone mastoidectomy 35 years earlier. The areas of the bone marrow and artefact were subtracted before calculating the total bone area.

There was a significant correlation between percentage lamellar bone and inter-operation time for all 21 malleus bones examined ($r = -0.512$, $p < 0.05$; Figure 2a). In contrast, there was no correlation between percentage lamellar bone and inter-operation time for any of the 20 incus bones examined ($r = -0.018$, $p = 0.941$; Figure 2b).

Discussion

Ossicles are miniature long bones, and histologically resemble other long bones such as the femur and humerus.⁷ They are covered with periosteum, exhibit a lamellar pattern, contain a Haversian system together with bone marrow and blood vessels, and are connected to each other via cartilage tissue. Little information is available regarding the histopathological changes in ossicles affected by chronic inflammation, presumably because such studies are already considered classical entities. In 1958, Grippaudo⁸ histologically examined 55 ossicles removed from 41 ears with chronic otitis media, and

concluded that the incus was more affected than other bones. In 1959, Pollock⁷ examined 31 ossicles from patients with chronic otitis media, and reported that the pathological findings were indicative of chronic osteomyelitis. More recently, Subotic and Femenic⁹ examined incus bones with cholesteatoma, and found that 67.5 per cent showed osteitis or osteomyelitis, such that intra-operative removal of the bone was recommended. The above studies were based on descriptive and qualitative analyses. To our knowledge, the present study is the first attempt to quantitate the histopathological changes in ossicles affected by chronic inflammation.

Interestingly, the percentage lamellar bone correlated with the inter-operation time only for malleus bones, not incus bones. From a pathological point of view, this finding suggests that inflammation plays a more significant role in the destruction of the malleus compared with the incus. In other words, the cause of malleus destruction is probably unifactorial (i.e. inflammation), whereas that of incus destruction is probably multifactorial.

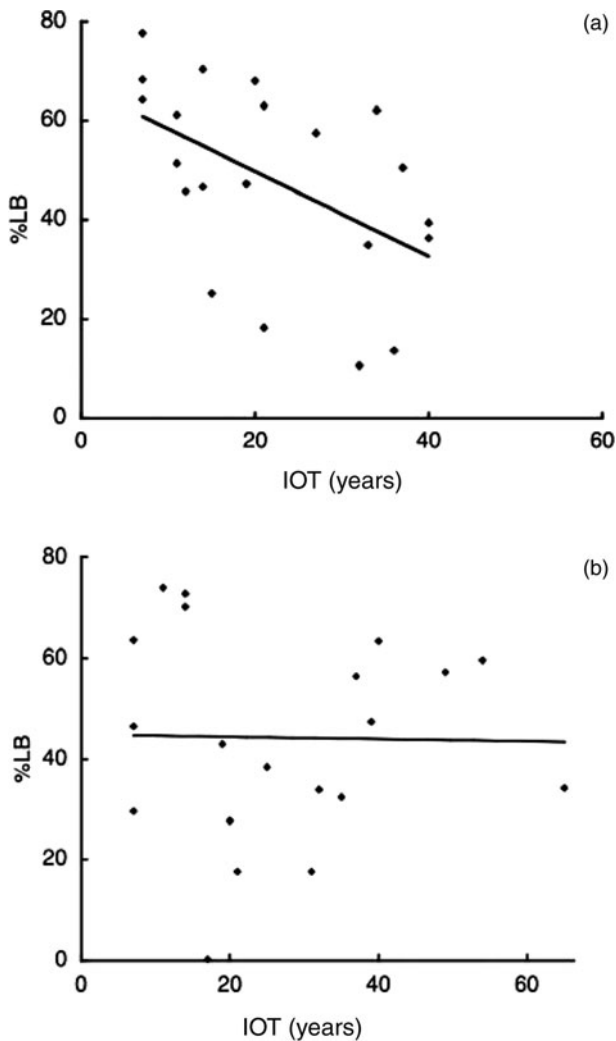


FIG. 2

Correlation between percentage lamellar bone and inter-operation time (IOT) for (a) the 21 malleus bones ($r = -0.512$; $p = 0.018$), and (b) the 20 incus bones ($r = 0.018$; $p = 0.941$).

It is widely known that the long process of the incus is more susceptible to avascular necrosis than other parts of the ossicles, including the malleus.¹⁰ Schuknecht¹¹ reported that resorption osteitis of the ossicles is common in cases of chronic otitis media, and occurs (in descending order of frequency) in the long process of the incus, the crura of the stapes, the body of the incus, and the malleus. The position and shape of the incus may also account for its vulnerability. The incus hangs in mid-air inside the middle ear, between the malleus and the stapes, with little direct contact with the middle-ear wall, and this can result in ischaemia.¹⁰ The long, slender shape of the long process of the incus makes it fragile, and hence vulnerable to external force.

Considered together, the above studies and our own findings suggest that the cause of destruction of the incus includes various processes of inflammation, ischaemia and external force. In comparison, the malleus is fixed firmly to the tympanic membrane and is less prone to factors such as ischaemia and

external force. Thus, one could assume that the main cause of malleus destruction would be inflammation.

We also investigated the pathological relationship between two ossicles obtained from the same ear. In our study, the malleus and incus were both harvested from each of 10 ears. Examination of these paired samples showed no significant correlation between malleus percentage lamellar bone and incus percentage lamellar bone ($r = 0.455$, $p = 0.186$), suggesting limited pathological relationship between these two bones.

- **Chronic ear infection with purulent discharge is often seen in patients who have previously undergone radical or modified mastoidectomy**
- **Total middle-ear reconstruction is indicated for such patients, mainly to improve their cavity problem and coexisting hearing loss**
- **Direct inspection of surgically removed ossicles from patients with long-term cavity problems often reveals increased destruction of the malleus in patients with a longer duration of cavity problems, whereas the degree of incus destruction does not appear to correlate with the duration of cavity problems**
- **The results of this histopathological study appear to confirm these impressions**

One limitation of the present study was that the choice of percentage lamellar bone and inter-operation time as study parameters depended merely on our subjective impression. Another limitation was the use of a single section selected from each ossicle for histological examination. It is possible that the selected sections did not represent the whole ossicle in terms of lamellar bone destruction. Likewise, the inter-operation time parameter represented only an approximation of the duration of the patient's cavity problem, rather than the exact duration of inflammation; the latter parameter would have been preferable, although unfortunately not measurable.

While these issues may limit the reliability of our results, we believe that our findings still warrant further investigation of the pathological mechanism of ossicular destruction.

References

- 1 Ekvall L. Total middle ear reconstruction. *Acta Otolaryngol* 1973;**75**:279–81
- 2 Sasaki T, Xu A, Ishimoto S, Ito K, Yamasoba T, Kaga K. Results of hearing tests after total middle ear reconstruction. *Acta Otolaryngol* 2007;**127**:474–9
- 3 Ishimoto S, Ito K, Sasaki T, Shinogami M, Kaga K. Total middle ear reconstructive surgery for the radicalized ear. *Otol Neurotol* 2002;**23**:262–6
- 4 Ishimoto S, Ito K, Shinogami M, Yamasoba T, Kaga K. Use of cartilage plate as tympanic membrane in total middle ear reconstructive surgery for infected radicalized ear. *Otol Neurotol* 2003;**24**:2–5
- 5 Xu A, Ishimoto S, Ito K, Yamasoba T, Kaga K. Assessment of total middle ear reconstruction by patient survey correlated with clinical findings. *Auris Nasus Larynx* 2003;**30**:15–20

- 6 Bullough PG. *Bullough and Vigorita's Orthopaedic Pathology*, 3rd edn. London: Mosby-Wolfe, 1997;15–17
- 7 Pollock FJ. Pathology of ossicles in chronic otitis media. *AMA Arch Otolaryngol* 1959;**70**:421–35
- 8 Grippaudo M. Histopathological studies of the ossicles in chronic otitis media. *J Laryngol Otol* 1958;**72**: 177–89
- 9 Subotic R, Femenic B. Histological changes of incus with cholesteatoma in the attic. *Acta Otolaryngol* 1991;**111**: 358–61
- 10 Alberti PW. The blood supply of the long process of the incus and the head and neck of stapes. *J Laryngol Otol* 1965;**79**:964–70
- 11 Schuknecht HF. *Pathology of the Ear*, 2nd edn. Philadelphia: Lea & Febiger, 1993;203–4

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