INITIAL INVESTIGATION OF THE EFFICACY AND BIOSAFETY OF SODIUM HYALURONATE (HEALON) AS AN AID TO ELECTRODE ARRAY INSERTION

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INTRODUCTION

Stimulation of residual neural elements by electrodes inserted into the cochlea to produce the perception of speech and environmental sounds in profoundly deaf people is a fundamental aim of cochlear implantation. The multiple-channel cochlear implant utilizes the tonotopic arrangement of the organ of Corti to also achieve place pitch perception by stimulating different electrode bands. It may be possible to improve the range of pitches perceived by present cochlear implant patients by inserting the electrode array more deeply.

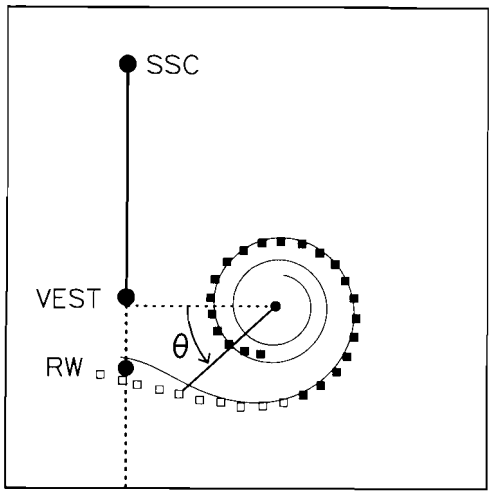

Fig 1. Example of digital reconstruction of plain film radiograph, showing anatomic reference points (superior semicircular canal [SSC] and vestibule [VEST]), angle θ used to specify positions of electrode bands, positions of electrode bands, and mathematical spiral fitted to data. RW — round window.

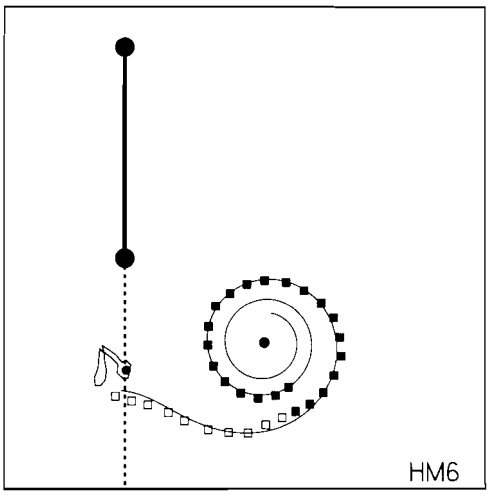

Fig 3. Example of digitally reconstructed radiograph. This temporal bone (HM6) had been implanted with Cochlear Pty Limited array using sodium hyaluronate. Note marker indicating position of round window.

To help achieve this, investigators have used sodium hyaluronate as a lubricant for electrode insertions.[1] It was felt deeper insertions were produced with sodium hyaluronate. Before introducing this substance as part of the surgical protocol for the Melbourne Cochlear Implant Clinic, it was decided to investigate its efficacy in aiding deeper insertions of the electrode. In addition, it was also necessary to determine if sodium hyaluronate, in conjunction with cochlear implantation, had adverse effects on the inner ear. This study was undertaken to address these issues.

METHOD

A temporal bone study was used to investigate the depths of insertion achieved using sodium hyaluronate as a lubricant. Six human cadaver temporal bones were implanted within 24 hours of death. The same surgeon who was experienced in implantation performed all the insertions. A standard surgical approach was used for access to the basal turn and a cochleostomy created. A drop of sodium hyaluronate was placed through the cochleostomy and a drop spread on the array before inserting the electrode. After insertion, the electrode was secured in place using a platinum wire tie. Four previously unused banded multiple-channel practice electrodes, with identical dimensions and properties to electrodes implanted in patients, were used. Two of the electrodes were used for two insertions, after carefully checking that the electrode was undamaged after the initial insertion. Each bone was then submitted to x-ray analysis to demonstrate the electrode within the cochlea.

Digitized images of the electrode were analyzed by computer, by means of a modification of a technique described by Marsh et al[2] to measure the angular depth of insertion of the individual bands (Fig 1). The insertion depth was designated as that of the most apical electrode band. However, with this initial study, because of time constraints, electrodes were not inserted into additional temporal bones without Healon as a control. A similar analysis of the radiographs of 22 patients

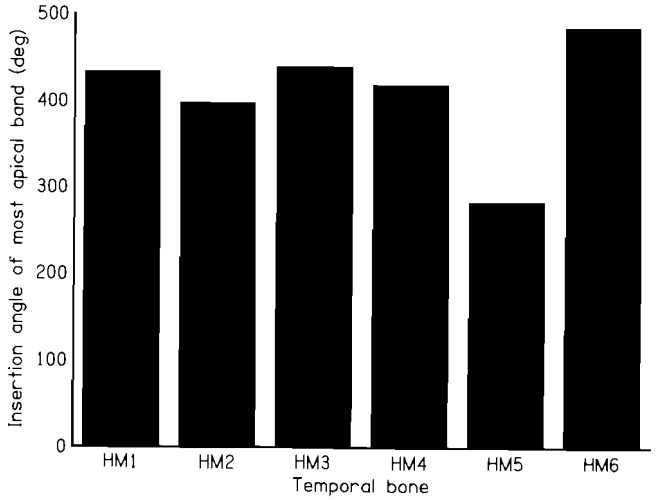

Fig 2. Insertion angles for most apical electrode bands of arrays inserted in temporal bones using sodium hyaluronate.

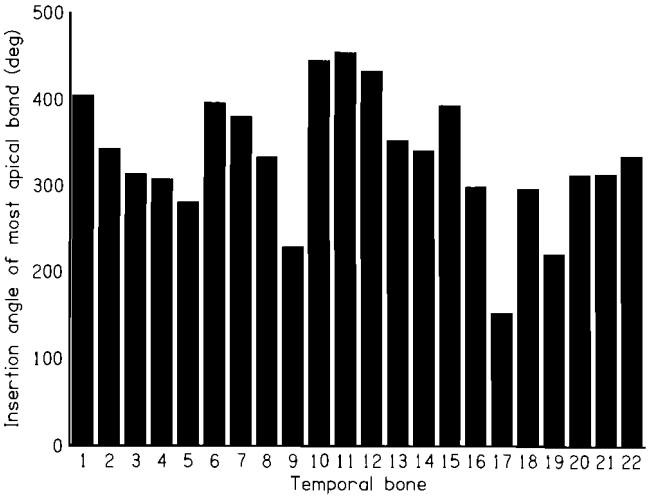

Fig 4. Insertion angles for most apical electrode bands of arrays inserted in 22 patients without use of sodium hyaluronate.

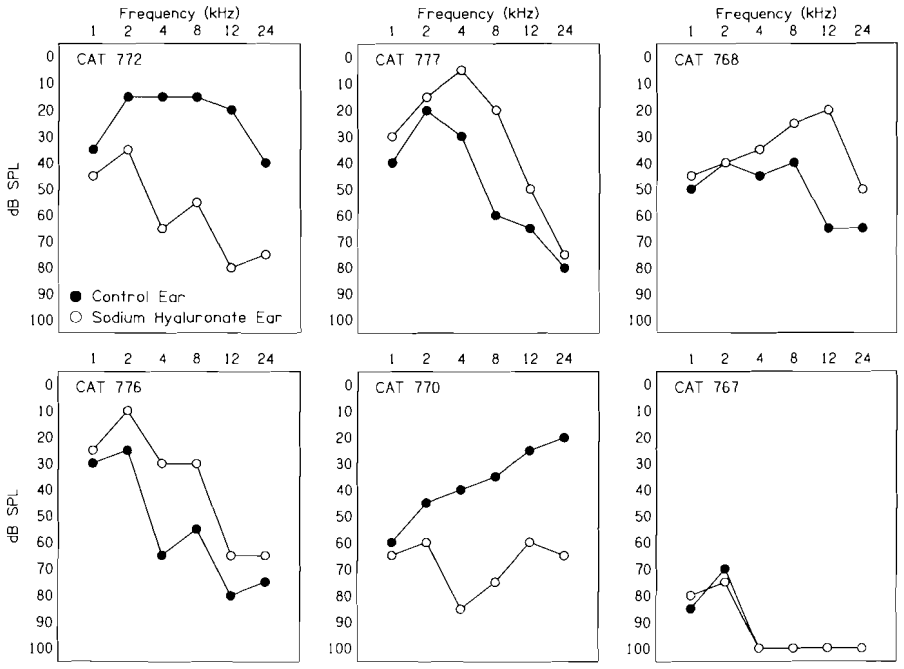

Fig 5. Audiograms constructed from frequency-specific auditory brain stem response data. Hearing thresholds for six cats, measured in two ears and at frequencies of 1, 2, 4, 8, 12, and 24 kHz. In each cat, one ear had been implanted with sodium hyaluronate, and other, without.

with patent cochleas implanted without the use of sodium hyaluronate was carried out as a control. As we have found with a previous temporal bone study that the average depth of insertion is less than that obtained at surgery, the temporal bone data present a worst-case situation (Clark, personal communication).

To investigate the biosafety of sodium hyaluronate, an animal study was undertaken. Six healthy cats with normal tympanic membranes and normal hearing thresholds, as assessed by click auditory brain stem response (ABR), were selected. Anesthesia was induced by intravenous ketamine and Rompun and an endotracheal tube was inserted. Under strict aseptic conditions the round window was exposed and the round window membrane opened. In one ear one drop of sodium hyaluronate was instilled through the round window. A dummy feline Silastic silicone rubber (Dow Corning Corp) electrode with four platinum bands with a drop of sodium hyaluronate spread on it was inserted through the round window. The other ear was also implanted with a dummy electrode with 0.9% sodium chloride solution used as a control. Throughout the procedure the animals' respiratory rate, end-tidal carbon dioxide and temperature were closely monitored. Anesthesia was maintained with intramuscular ketamine. A dilute solution of cloxacillin was instilled after implantation, and a long-acting intramuscular penicillin was given. Four months after surgery, frequency-specific ABR measurements at 1, 2, 4, 8, 12, and 24 kHz using tone pips were made to establish the hearing thresholds for both ears of each implanted cat. The cats were in a sound-proofed room during the measurements. This study was approved by the Animal Ethics Committee of the Royal Victorian Eye and Ear Hospital.

RESULTS

Insertion Distances. The maximum angular depths of the electrodes inserted into the temporal bones with use of sodium hyaluronate are shown in Fig 2. The mean depth of insertion was 411°. An example of the reconstituted radiograph of an inserted array is shown in Fig 3. In the control group of 22 patients implanted without the use of sodium hyaluronate, the maximum angular depth of insertion for each electrode is shown in Fig 4, with the mean being 335°. While these results suggest that significantly deeper insertions were obtained with sodium hyaluronate (Student's *t* test: $p = .034$), it should be pointed out that there were substantial differences between the two groups. The first group comprised temporal bones implanted by a single surgeon using sodium hyaluronate, while the second comprised patients implanted by various surgeons without sodium hyaluronate.

Hearing Thresholds. The frequency-specific ABR thresholds were converted to decibel (sound pressure level) thresholds by means of a calibration table. The hearing thresholds were plotted as audiograms (Fig 5). In cats 772 and 770 the hearing threshold was lower in the control ear than in the ear in which sodium hyaluronate had been used. Cats 777, 768, and 776 had lower hearing thresholds in the ear with sodium hyaluronate than in the control ear. There was no difference between the thresholds obtained for the two ears of cat 767. A two-tailed paired *t* test comparing the sodium hyaluronate and control thresholds for all six cats over six frequencies gave a p value of .013, indicating a significant difference between the sodium hyaluronate and control groups, with the former having lower thresholds. However, as three cats had lower hearing thresholds with sodium hyaluronate and two had higher thresholds, the loss of hearing is likely to be due primarily to the effects of surgery rather than to the test substance.

DISCUSSION

The insertion depth of the electrode generally achieved in cochlear implantation allows for stimulation of the auditory nerve fibers as far as the region of 1,000 Hz. As important speech information is contained at frequencies lower than this, it is desirable to achieve deeper insertions of the elec-

trode. Normally the electrode is inserted into the cochlea through a surgically created fenestration in the basal turn. The array is advanced until slight resistance is felt. Attempts to force the array more deeply can damage the cochlea and the electrode.[3] In an attempt to facilitate insertion of electrodes that were proving difficult to insert, German investigators began using a substance called sodium hyaluronate or hyaluronic acid.[1] Previous studies in which sodium hyaluronate was applied to a lesioned round window membrane did not reveal cochlear ototoxicity.[4,5] Not only did it seem to act as a lubricant, helping the electrode to glide into the cochlea, but it also appeared to allow the achievement of deeper insertions.

Sodium hyaluronate is a biologic substance found in the ground matrix of many tissues. It already has a number of clinical uses, chiefly in ophthalmology, where it is used in cataract surgery to maintain the volume of the anterior chamber and to protect the endothelium of the cornea. An attempt has been made to use it as a healing agent for reconstructive middle ear surgery, but no significant benefit was found with its use.[6]

Our study has shown that significantly deeper insertions may be achieved with sodium hyaluronate used as a lubricant, substantiating the original observations of Lehnhardt.[1] We have partly addressed the issue of biosafety in measuring the hearing thresholds after implantation. There was no deterioration in the thresholds that could be attributed to sodium hyaluronate. In fact, in three cats the thresholds were lower in the ears in which that substance had been used. This may be reflecting a cytoprotective effect of sodium hyaluronate.

Further work is necessary to assess morphologic changes in the cochlea associated with the use of sodium hyaluronate in cochlear implantation. In particular, it will be necessary to examine hair cell damage, loss of spiral ganglion cells, and the inflammatory reaction to the electrode. The cochleas of the cats used in the above study are being prepared for this investigation.

SUMMARY

Sodium hyaluronate has potential uses as an electrode lubricant in cochlear implant surgery. Deeper electrode insertions were achieved in six temporal bones implanted with sodium hyaluronate, compared to 22 patients implanted without sodium hyaluronate. Preliminary biosafety studies measuring hearing thresholds of six cats 4 months after implantation with dummy electrodes did not show evidence of ototoxicity caused by sodium hyaluronate. Until the biosafety studies are complete, we cannot recommend sodium hyaluronate for routine use, but the results so far are promising.

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