'Real-life' benefit of hearing preservation cochlear implantation in the paediatric population: a single-site case–control study

Iain Bruce, Simone Schaefer, Karolina Kluk, Jaya Nichani, Martin Odriscoll, Azita Rajai, Mark Sladen

ABSTRACT
Introduction Cochlear implantation with hearing preservation (HPCI) has allowed a cochlear implant (CI) electrode to be implanted while trying to preserve residual acoustic low-frequency hearing. The concept arises from the importance of this low-frequency information and the limitations of a CI in several auditory domains. The combination of electrical hearing with either preserved acoustic hearing or amplified ‘natural’ hearing has the potential to address these issues and enable children with HPCI to closely follow normal auditory development. The aim of this study is to evaluate the ‘real-life’ benefit of preserved acoustic low-frequency hearing in children with a CI, understand the benefits of preserved natural hearing in complex listening situations and so enable parents and children to make an informed choice about implantation. Ultimately, helping to ensure the maximum number of children benefit from this life-changing intervention.

Methods and analysis Nineteen ears in children and young people aged 6–17 years old with ‘successful’ HPCI will be subjected to a test battery consisting of: (1) spatial release from masking; (2) complex pitch direction discrimination; (3) melodic identification; (4) perception of prosodic features in speech and (5) threshold equalising noise test. Subjects will be tested in the electro-acoustic stimulation (EAS)/electro-natural stimulation (ENS) and the electric-only (ES) condition, thereby acting as their own control group. Standard demographic and hearing health information will be collected. In the absence of comparable published data to power the study, sample size was determined on pragmatic grounds. Tests are exploratory and for hypothesis-generating purposes. Therefore, the standard criterion of p<0.05 will be used.

Ethics and dissemination This study has been approved by the Health Research Authority and NHS Research Ethics Committee (REC) within the UK (22/EM/0017). Industry funding was secured via a competitive researcher-led grant application process. Trial results will be subject to publication according to the definition of the outcome presented in this protocol.

INTRODUCTION
Cochlear implantation with hearing preservation (HPCI) has allowed a cochlear implant (CI) electrode to be implanted while trying to preserve residual acoustic low-frequency hearing.1–3 Theoretically, successful hearing preservation (HPCI) allows patients to perceive sounds via the CI electrode and their own cochlea, providing them with access to any residual ‘natural’ low-frequency hearing. The concept arises from our understanding of the importance of this low-frequency information and the limitations of a CI in several auditory domains.4 Despite technological advances in CI systems, the amount of speech information available for children with a CI compared with their normal hearing peers or conventional hearing aid wearing peers is limited.3,5–6 These differences become particularly apparent in challenging situations, such as noisy environments or in the presence of competing sounds. Furthermore, for some features of speech that are essential for communication, such as stress, intonation and emphasis the perception of which can be significantly impaired in paediatric CI users.4 In addition, music perception is poor in this group, which can have consequences for development and social interaction.7
loss, children who were implanted performed much better than those using traditional hearing aids. They showed a steep improvement in speech perception a year after implantation compared with pre-implant.8

Based on the evidence derived from our recent systematic review, the combination of electrical hearing, that is, CI, with preserved acoustic hearing within the ipsilateral ear—either with acoustic amplification (electro-acoustic stimulation (EAS)) or without amplification (electro-natural hearing (EN))—could have the potential to address these issues and enable children with HPCI to more closely follow a normal course of auditory development.9 The understanding of the factors influencing successful HPCI is increasing, including surgical skill and technique, steroid usage, ‘patient factors’ and the physical characteristics of the electrode.

Clinical evaluation of the benefits following HPCI so far has focused on ‘standard’ tests designed to test function in optimised conditions. Failure to understand and capture any ‘real-life’ benefits of preserved acoustic hearing risks missing or underestimating benefit in day-to-day life. Furthermore, to date the uptake of EAS audio-processors in children has been limited. The mechanisms and reasons behind this are poorly understood but could have substantial consequences for the management and counselling of children with HPCI. Greater understanding of the benefits and limitations of EAS and electro-natural stimulation (ENS) is critically important if children and young people (CYP) with borderline hearing thresholds (either with or greater than 80 dBHL at two or more frequencies) are to receive balanced information and individualised care. In the UK, the eligibility criteria for CI have been broadened to include patients with hearing loss equal to or greater than 80 dBHL at two or more frequencies. Countries including Germany, Saudi Arabia and Australia have flexibility in their guidelines to include children with cut-off thresholds at 70 dBHL or below.9 10 Lack of understanding of the effect of combining electric and acoustic hearing is in part responsible for this variability in practice. The next challenge in the evolution of HPCI is to better understand the real-life benefits of preserved natural low-frequency hearing to support informed choice about implantation, especially now that HPCI will become an option for an increasing number of CYP. Accomplishing this will ensure that the maximum number of CYP could benefit from this life-changing intervention.

Study aim
The aim of this study is to evaluate the ‘real-life’ benefit of preserved acoustic low-frequency hearing in children with a CI, resulting in better understanding of the benefits of preserved natural hearing in complex listening situations. Accomplishing this would represent an important step towards truly meaningful shared decision-making in those with borderline hearing thresholds. We hypothesise that children with preserved low-frequency hearing following cochlear implantation display better outcomes in complex listening situations when using electro-acoustic or electro-natural vs electric-only hearing.

Primary objective
1. To meaningfully evaluate the ‘real-life’ benefit of preserved low-frequency acoustic hearing in children with CI using a test battery.
2. To evaluate the effect of accounting for HP in CI programming (ie, child’s preferred programming settings) on real-life benefit from HP in children with HPCI. Comparison of subjects whose CI is programmed without reference to residual hearing thresholds vs subjects whose CI is programmed with reference to residual hearing thresholds.

Secondary objective
1. To evaluate compliance to the study protocol test battery, the number of tests fully completed.

METHODS AND ANALYSIS
This is a single-site, case-control, observational study with prospective data collection that does not involve any change from standard care. Within-subject single measure design with five outcome domains tested for each subject. Participants will act as their own controls, avoiding bias from poor matching.

Subjects will be selected from our database of paediatric patients who have undergone cochlear implantation with hearing preservation (HP) at the Royal Manchester Children’s Hospital. If they meet the inclusion/exclusion criteria (see table 1), trained research personnel will obtain informed consent (and assent if appropriate) from the patient/parent (see online supplemental materials 1–3).

The research audiologist will prospectively perform all hearing assessments for each participant in the following conditions:

- Control condition: electrical hearing (EN), which entails EN with ear canal plugged off with an ear plug
- Test condition: electro-natural hearing, which entails EN+use of natural hearing (ENS) or EAS, which entails EN+use of acoustic amplifications. This is based on the participant’s typical hearing configuration.

The test order is randomised to limit the effect of fatigue.

Spatial release from masking
To simulate complex auditory environments with competing sounds, participants will be tested on spatial release from masking. Targeted speech will be presented from the front (0°) with the masker coming from the front (0°) or the side of the implanted ear (90° or −90° depending on unilateral or bilateral implantation) (figure 1). Speech perception will be tested by the McCormick automated toy test for children younger than 7 years of age and the Bamford-Kowal-Bench (BKB) sentence test for children older than 7 years of age (depending on child’s cognitive abilities) with a starting signal level of 60 dBSPL. To measure speech-reception thresholds (SRTs), the competing noise will be fixed at 60 dBSL throughout the test.
Complex pitch direction discrimination test
The pitch direction test is implemented using a two-alternative, forced-choice test with one-up, one-down adaptive tracking. On each presentation, a tone at the reference F0 and a higher-pitched tone determined by the adaptive interval size is played in random order. Stimuli is presented from the front (0°) loudspeaker 1 metre away. The users are asked to identify which note was higher in pitch. The minimum tested interval is 1 semitone (approximately 6% F0 difference), and the maximum is 12 semitones or 1 octave (100% increase in F0). To create an accurate psychometric function, a reversal at zero is automatically added by the test algorithm when the user answers correctly at 1 semitone. Adaptive tracking is performed simultaneously with samples from three base frequencies (262 Hz (C4), 330 Hz (E4) and 391 Hz (G4)) interleaved in random order, until 3 trials of 8 reversals for each base frequency are completed. The threshold values for each base frequency are calculated separately by using the mean of the last six reversals for each trial and averaging the results from the three trials into a final threshold for discrimination of synthetic complex pitch direction change. The duration of the test varies according to the responses of the participant. On average, the test should take 20 min to complete (10 min for control setting and 10 min for test setting) (figure 2).

Melodic identification test
Stimuli: A melody clip (total of 12), for example, Old MacDonald or Twinkle Twinkle Little Star tune is randomly presented (each melody is presented three times). Stimuli is presented from the front (0°) loudspeaker 1 metre away. Each tone has a 500 ms duration and are presented at a tempo of 60 beats per minute. The amplitude of each note in the melody is randomly varied by ±4 dB, and five different versions of each melody are pre-recorded. One version is randomly chosen each time the melody was presented, and all melodies are truncated at 8 s to prevent song length providing a potential cue. To eliminate rhythm cues for melody recognition, the melodies are created by repeating all longer notes in an eighth-note pattern, yielding isochronous melodies. The final score is reported as a percentage of correct response on the melodies with which the listener is familiar. (figure 2).

Perception of prosodic features in speech
To determine the subject’s ability to pick up on prosodic features of speech, an in-house test was developed by our lead speech and language therapist consisting of a voice recording of 10 sentences. One sentence at a time is played and the participant has to circle/underline the stressed word in the sentence on a sheet of paper with the sentences written down. The stressed word is often described to the participant as the important word in the sentence. Participants have to be literate to complete the test, although further applications are considered with pictures replacing written words. An initial pilot study revealed normal hearing subjects outperforming bilateral CI subjects, with both outperforming unilateral CI participants (figure 2).

Threshold equalising noise (TEN) test
Cochlear dead regions can be diagnosed using threshold equalising noise (TEN) test by measuring masked
threshold of a pure tone presented in the background of a spectrally shaped masker. The masker level is held constant and the signal level is adjusted to obtain the masked thresholds. TEN level is set to the highest acceptable level −5 dB. Testing is only done at thresholds of 500 Hz, 750 Hz and 1000 Hz, given that higher frequencies are not of relevance with regard to low-frequency HP (125 Hz and 250 Hz are not part of the TEN test software). If for a specified frequency the masked threshold is 10 dB or more above TEN level, and the difference between masked and absolute threshold is ≥ 10 dB, the result indicates presence of a death region at this frequency. The duration of the test is approximately 30 min. The TEN test is also validated for use with children as young as 8 years old. The inclusion for the study is 6 years old, therefore those below this age within our population will not complete the test.

**Statistical analysis plan**

In the absence of previous information to power the study, sample size was determined on pragmatic grounds. Tests are exploratory and for hypothesis-generating purposes. Therefore, the standard criterion of p<0.05 will be used rather than corrected for multiple test effect.

Appropriate descriptive analysis of participants’ demographics and baselines will be provided. The number (%) of participants who completed each part of the tests will be reported. Numeric outcome measures will be summarised for each test condition using mean/median (SD/IQR) depending on the distribution. Binary outcomes will be summarised by count (%).

**Outcome domain 1: spatial release from masking**

SRT score in control and intervention condition (numeric).

Two-way repeated measures analysis of variance (ANOVA) with two factors (hearing modality; direction of sound) both with two levels (hearing modality: CI only (control) vs CI+acoustic hearing (intervention); direction of sound: front 0 degrees vs ipsilateral 90 degrees) with the outcome being mean SRT.

**Outcome domain 2: complex pitch direction discrimination test**

Interval size in control and intervention condition (numeric 0–12).

Two-way repeated measure ANOVA with two factors (hearing modality; base frequency) with two and three levels (hearing modality: CI only (control) vs CI+acoustic hearing (intervention); base frequency: 262 Hz (C4, or middle C), 330 Hz (E4), and 391 Hz (G4)) with the outcome being mean per cent score correct.

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Figure 1  Loudspeaker layout relative to the subject for spatial release from masking test. Two of the three speakers were used for each subject depending on which ear was tested (front and left or right). With target speech plus noise from the front (0°) loudspeaker only followed by target speech only from the front (0°) loudspeaker and noise only from the left (−90°) or right (+90°) loudspeaker. The subject has to repeat target speech. HPCI, cochlear implantation with hearing preservation.

Figure 2  Loudspeaker layout relative to the subject for the complex pitch direction discrimination, melodic identification and perception of prosodic features in speech test. Stimuli from the front (0°) loudspeaker. The subject provides a response using the laptop situated in front of them.
Outcome domain 3: melodic identification test
Correct response score in control and intervention condition (numeric/percentage 0–100).
Paired t-test.

Outcome domain 4: prosodic features in speech
Number of words correct in control and intervention condition. (numeric/percentage 0–100).
Paired t-test.

Outcome domain 5: dead region testing descriptive statistics for presence or absence of dead region
Cochlear dead regions present or not in control and intervention condition. (binary yes/no).
McNemar test.
A follow-up t-test will be performed to investigate differences in mean found by ANOVA.
Inference criteria: Number and percentage of participants completing the test and its 95% CI will be calculated.
Data exclusion: Outliers will be included in the analysis.
Missing data: Due to differences in cognitive development, children might not be able to participate in a test despite meeting the age criterion. Furthermore, the TEN test has been shown to be validated upwards from 8 years of age, therefore those below this age within our population will not complete the test and excluded from analysis. Therefore, sample size between tests might vary.
If a patient cannot participate in the test, they will be excluded from analysis for that particular subtest.
The data generated by the study will be analysed at Manchester University NHS Foundation Trust and the analysis will be performed by researchers employed by Manchester University NHS Foundation Trust.

Patient public involvement
The Children’s Cochlear Implant Support group (CICS, Website: www.cicsgroup.org.uk) was consulted in the design of study documentation, review of the Patient Information Sheet (PIS).
Study results will be disseminated via the CICS social media channels and mailing lists.

Methodological summary
The concept and desire for preserving natural low-frequency hearing is based on our understanding of the importance of low-frequency information to various auditory domains, for example, speech in noise and music perception. Current CI devices cannot offer detailed levels of frequency resolution, representation of input signals or representation of fundamental frequencies that acoustic hearing can. This results in decreased speech discrimination in noise, music perception as well as poor interpretation of speech stress and intonation in CI users. Successful HPCI has the potential to provide the benefit of electric stimulation without losing the characteristics of low-frequency acoustic hearing, overcoming the aforementioned limitations of the CI-only condition. Adding this acoustic signal to the electric stimulation from the CI could lead to improved outcomes on various audiological domains that are used in complex real-life listening situations. Yet, the literature fails to provide conclusive evidence regarding the specific benefit of acoustic hearing in addition to CI in complex listening.

Our systematic review found evidence highlights that HCPI benefits listening in background noise and music and that there does not appear to be significant benefit from preserved natural hearing for speech in quiet. Therefore, for our study we have chosen a ‘real-life’ test battery including speech, music and speech stress/intonation.

Data storage and security
Data will be stored on Manchester University NHS Foundation Trust’s network drives with firewalls and security measures in place. Hard copy records will be stored in a locked cabinet in a secure location. Access to records and data will be limited to study personnel who are also part of the clinical care team. Study data will be de-identified and a master linking log with identifiers will be kept and stored separately from the data.

ETHICS AND DISSEMINATION
This study has been reviewed within the funding organisation (Cochlear Research and Development Limited), by an independent and relevant peer reviewer/committee. Favourable comments and approval of the protocol were given from the peer review process. A favourable opinion has also been granted by the Health Research Authority (HRA) and NHS Research Ethics Committee (REC) for the study and all the supporting documents including this protocol, information sheets, informed consent forms and other relevant documents (22/EM/0017).
Study results will be disseminated via the CICS via, for example, newsletters, social media, as deemed appropriate by the charity and mailing lists. A summary of study results will be provided to all participants who have consented to be contacted regarding the study results. Aim for publication of the final study results in medical literature and presentation on medical conferences.

There is also an intention to share an anonymous final data set with external researchers; however this will only occur if the correct data sharing agreement is in place.

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Contributors The study concept and design were conceived by IB, SS, KK, JN, MO, AR and MS. IAB is the chief investigator who secured funding together with SS and MO. MS will conduct recruitment, screening and data collection. The statistical analysis plan was authored by AR and will be performed by AR, IB, SS, MO and MS prepared the first draft of the manuscript. All authors provided edits and critiqued the manuscript for intellectual content.
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Competing interests None declared.
Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES
CONSENT FORM for Patients

Title of Project: The 'real-life' benefit of hearing preservation cochlear implantation in the paediatric population

IRAS ID: 310398

Study Number: B01072

Participant Identification Number for this trial:

Name of Researcher: Prof Iain Bruce

1. I confirm that I have read the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had them answered satisfactorily.

2. I understand that my participation/the participation of my child is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

3. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

4. I understand that the information collected about me will be used to support other research in the future and may be shared anonymously with other researchers.

5. I agree to take part/ for my child to take part in the above study.

Hearing Preservation - Consent Form for Patients V2.0 02/02/2022
IRAS Number 310398
Optional Questions

I agree to be contacted with study results

I agree to be contacted for clarification of my data/my child’s data at a later date, if required.

My preferred contact (please tick and include email if preferred)

Do not contact  Phone  Post  Email

________________________  ____________________________  ____________________________
Name of Participant  Date  Signature

________________________  ____________________________  ____________________________
Name of Person taking consent  Date  Signature

When Completed 1x original – into Site File; 1x copy – to Participant; 1x copy – into medical records
CONSENT FORM for Parents/Carers

Title of Project: The 'real-life' benefit of hearing preservation cochlear implantation in the paediatric population

IRAS ID: 310398

Study Number: B01072

Participant Identification Number for this trial:

Name of Researcher: Prof Iain Bruce

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My preferred contact (please tick and include email if preferred)

Do not contact  Phone  Post  Email __________________________

__________________________
Name of Participant

__________________________  __________________________  __________________________
Name of Parent/Carer  Date  Signature

giving consent

__________________________  __________________________  __________________________
Name of Person  Date  Signature

taking consent

When Completed 1x original – into Site File; 1x copy – to Participant; 1x copy – into medical records
IRAS ID: 310398

Participant Identification Number:

**ASSENT FORM for Participants aged 6-15 years old**

Title of Project: The 'real-life' benefit of hearing preservation cochlear implantation in the paediatric population.

Name of Lead Researcher: Prof Iain Bruce

Please tick the boxes below

1. I understand what this project is about.  

2. I have asked all the questions that I want.  

3. All my questions have been answered in a way I understand.  

4. I understand that I can decide whether to take part or not and can change my mind at any time.  

5. I am happy to take part in the study.  

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Thank you for your help.

IRAS ID: 310398, Assent Form for participants 6-15 years old, V 1.0, 13 Sep 2021