Abstract
The purpose of this paper is to present the experimental protocol and the work in progress performed in the framework of the European project GUARD to assess potential changes of the hearing function of humans after exposure to low-intensity electromagnetic fields produced by GSM cellular phones. Pilot studies have confirmed the practicality of the protocols. The study design, test protocols and preliminary analysis of data from the first recordings will be presented.

Key Words
biological effect of electromagnetic radiation; auditory system; distortion product otoacoustic emissions.

1. Introduction
Mobile phones have become very commonly used throughout the world within a short period of time. Although there is no clear evidence to show harmful physiological effects of electromagnetic fields (EMF) at the levels used by mobile phones, there is widespread public concern that there may be potential for harm. Therefore, it is appropriate to conduct sensitive studies to allay any public concern. Such studies should employ methodology that is able to detect very small effects with appropriate statistical power.

Because mobile phones are usually held close to the ear, it is appropriate to study effects on hearing. The external ear provides a natural route by which EMF emitted by mobile phones may reach the peripheral and central nervous system without severe attenuation by the bone of the skull. Moreover, the outer hair cells (OHC) of the cochlea are exquisitely sensitive and relatively easily damaged by excessive sound exposure. It is possible that EMF may modify the uptake of toxic agents produced during activation of these inner ear structures. There is the potential for the combined sound and EMF exposure to interact, aggravating the potential for damage to the outer hair cells. However, to date there is a limited knowledge on potential adverse effects of GSM cellular phones on human hearing [1, 2, 3].

2. Materials and Methods
Experimental paradigms
In this study two experimental paradigms are used: the within-subject paradigm and the between-subject paradigm. The first entails measurements immediately before and immediately after exposure to EMF via a commercial mobile phone. The procedure is conducted twice in a double-blind design: once with a genuine exposure and once with a sham exposure. This approach maximises sensitivity to change because between subject variation in the results is minimised by calculating the difference between before and after measurements. However practical and ethical considerations impose severe restraints on the intensity and duration of exposure that can be allowed. Therefore, exposure dose is necessarily low and such studies may miss important chronic effects. For this reason, the human studies include two parallel strands of investigation: longitudinal assessment of acute effects of short-term exposure (within-subject study) and cross-sectional comparison of groups of mobile telephone users (between-subject study). The latter strand utilises two groups: heavy users and light users of mobile telephones. The differences between groups are assessed to determine if there may be any chronic effects of mobile telephone use.
Participants and screenings
Participants are healthy young adults (18-30 years old) without any evidence of hearing or ear disorder, corresponding to the standard definition of otologically normal. Absence of pre-existing hearing or ear disorder maximises the sensitivity of the study to detect small changes that may occur. Acceptance as participants is based on otoscopy, audiometry by air conduction (0.5, 1, 2, 3, 4, 6, 8 kHz) and bone conduction (0.5, 1, 2 kHz), tympanometry and acoustic reflex testing, and a simple screening questionnaire concerning medical and otological history.

Additionally, for the between-subject study, participants are screened either as high or as low users of mobile telephones, where high users are defined as typically speaking for at least 30 minutes per day using a mobile phone held to the ear and low users are defined as typically speaking for less than 5 minutes per day.

Assessment of auditory function
The tests for assessment of auditory function are: transient otoacoustic emissions (TEOAE) using click stimuli, distortion product otoacoustic emissions (DPOAE) using DP-gram and I/O function, auditory brainstem response (ABR) using clicks at medium and high rates. Optionally, contralateral suppression of TEOAEs and DPOAE microstructure sweep are performed. For the within-subject study, they are performed immediately before and after exposure to EMF and only the exposed ear is tested. For the between-subject study, they are performed only once on both ears. All testing is carried out in a sound-treated room or booth satisfying criteria in ISO 8253-1 for air conduction audiometry using earphones down to 0 dB HL.

TEOAEs are recorded according to the so-called “linear protocol” [4] at 60, 70 and 80 dB. Each measurement run includes a minimum of 500 sweeps (i.e. 2000 clicks). DPOAE are recorded with the frequency ratio F2/F1 set equal to 1.22. Primary tone levels L1 and L2 are 60 and 50 dB respectively. The tones are swept with F2 covering the range 2 to 8 kHz in 1/16-octave steps. For each step, measurement of the DPOAE utilises signal averaging for 6 seconds, or until a signal-to-noise ratio of at least 15 dB is reached, whichever occurs first. For the within-subject study only, an input-output (I/O) function is measured for F2=2 and 4 kHz and the following combinations of L1 and L2: 50/35, 55/40, 60/50, 65/60, 70/70. These combinations approximate the scissors-level paradigm of Kummer et al. [5]. Additionally, for the between-subject study, the F2 sweep measurement are repeated for the following combinations of L1 and L2: 50/35, 55/40, 65/60, 70/70. This also allows input-output (I/O) functions to be determined for every frequency.

ABR is recorded with recording electrodes positioned on the vertex, ipsilateral mastoid and contralateral mastoid. Stimuli are 0.1 ms broadband clicks presented at an intensity level of 93-dB peak-equivalent SPL. Two click rates are used: 33.1 and 74.1 per second with filter settings 100 Hz (high-pass) and 3000 Hz (low-pass). Recordings entail averaging the responses from 2000 clicks at each rate. The amplitudes and latencies of waves I and V and the ABR are measured. The rationale is to test the refractory behaviour of the auditory nerve and brainstem under a high rate of stimulation. The difference in magnitude of response (e.g. wave V) at the two rates gives an indication of the ability of the nerve to sustain high rates.

Exposure and positioning system: within-subject study
The exposure, double blind and counterbalanced in order, consists of speech at a typical conversational level delivered via an earphone to one ear, plus EMF exposure in either genuine (test) or sham (control) conditions to simulate the normal use of a phone. Genuine and sham exposures are on separate days (at least 24 hours apart) with the test participant and tester both blind to the condition being used. To prevent any possible effects, from using the speaker in the handset the speech material is delivered via a ER-3A insert phone. The insert phone is used without the eartip inserted and the tube is taped along the subject’s jaw with the entrance of the tube placed at the tragal notch of the subject.

EMF exposure utilises the normal output of a consumer mobile phone (NOKIA 6310) at full power for 10 minutes. Half of the participants receive GSM exposure at 900 MHz (full power = 2W) and the other half receive GSM exposure at 1800 MHz (full power = 1W). The mobile phone is connected via serial data cable from the PC to the phone and running software to set the exposure parameters to the required frequency (900 or 1800 MHz) and required power.

The sham or genuine exposure is performed using a “load” or a “dummy load” (Fig. 1). The “load” intercepts the RF signal to the internal antenna on the phone and dissipated the RF in the load, while the “dummy load” looks identical but does nothing, allowing the RF to reach the antenna.

A system of phone fixation with a possibility of freely moving of the subjects’ head was designed. Therefore the positioning holder has three main parts: a headband, an adjustable arm and the phone holder (Fig. 2). All parts of the positioning system were made by non-metallic plastic materials in order to avoid any perturbation of the EMF emitted by the mobile phone. The headband allows free movement of the head without any replacement of the phone from the adjusted position. By using the adjustable arm the phone may be placed into the required position and may be adjusted according to the size of the subject under investigation.
The adjustable arm can be placed on both side of the headband. The phone holder is placed on the battery-side of the phone. In this way the weight of the holder may be kept as light as possible. During the exposure the phone is placed so that its longitudinal axis follows an imaginary line from the entrance to the ear canal to the corner of the mouth.

Statistical analysis
For the within-subject study, in addition to descriptive analysis of the data, differences in the measures obtained before and after exposure are compared between the genuine and the sham exposure using Student’s t-test for related samples and repeated-measures analysis of variance (p-value set at 0.05). Hearing threshold levels and other data obtained at the screening stage are used as covariates. In the between-subject study, besides the descriptive analysis of the data, the high user and low user groups are compared using Student’s t-test for independent samples and analysis of covariance. Hearing threshold levels and other data obtained at the screening stage, and detailed noise exposure estimates, are used as covariates (p-value set at 0.05).

3. Results
A pilot study (three subjects) was implemented to rule out any problems with the test procedures required for the GUARD project. All mobile phones included in the project have passed validation tests before use. During the tests the power, the frequency and the spatial distribution of the radio frequency exposure was processed. In Figure 3 an example of the Specific Absorption Rate (SAR, W/kg), distribution on one layer within the head phantom is represented. In all cases the SAR was below 2W/kg which is the limit of the European recommendation. In the case of the within-subject study, the first session (with screening) takes just under 2 hours and the second session about 1 hour 40 minutes. This time has been judged acceptable to the subject. For the between-study the duration of the recording is not so crucial considering that there is no an exposure session.

In Figure 4 and Figure 5 a mean high-resolution DP-gram recorded before and after the real and sham exposure, respectively, is reported as an example.

The variation in results appears small at this stage (although subject numbers are too small for statistical analysis) and individual variability is within the limits at which the effect should be notified to the ethics committee. Note that the apparent pre-post difference in Figure 5 occurs for the sham exposure.
4. Conclusion

The rapid worldwide increase in the use of mobile phones raises questions about possible adverse effects of the EMF emitted. Of all anatomical structures, the ear is in closest proximity to the mobile phone. This may lead to relatively high energy deposition in the ear compared to other parts of the body. Although the effect of mobile phones on hearing aids has been studied [6] there has been no systematic investigation on hearing itself. The aim of the European Project GUARD is to assess potential changes in auditory function as a consequence of exposure to low-intensity electromagnetic fields produced by GSM mobile phones at frequencies of 900 and 1800 MHz.

The pilot study performed at the Institute of Sound and Vibration Research (ISVR) at the University of Southampton, has confirmed the practicality both of the study design and of the test protocols. No problems were found with performing the two recording and exposure sessions. The longest test session is around 2 hours. The results of the GUARD project will be available at the end of 2004.

5. Acknowledgement

This work was supported by fund from the European Project GUARD “Potential adverse effects of GSM cellular phones on hearing” (FP5, QLK4-CT-2001-00150, 2002-2004). The authors wish to thank Dr. Sakari Lang from the NOKIA Research Center in Helsinki, for the assistance in the development of the exposure system.

References