PROJECT FINAL REPORT

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[1] Usually the contact person of the coordinator as specified in Art. 8.1. of the Grant Agreement.

[2] The home page of the website should contain the generic European flag and the FP7 logo which are available in electronic format at the Europa website (logo of the European flag: http://europa.eu/abc/symbols/emblem/index_en.htm logo of the 7th FP: http://ec.europa.eu/research/fp7/index_en.cfm?pg=logos). The area of activity of the project should also be mentioned.

4.1 Final publishable summary report

Executive summary (max 1 page)

Just thirty-five years ago there were no effective treatments for deafness or severe hearing impairment. The advent of cochlear implants (CIs) changed that, and today implants are widely regarded as one of the great achievements of modern medicine.

However, the extent of the electrical stimulation and its effect on the brain is not well known. This, combined to the lack of pre-operative measures that predict the outcomes after implantation, results in high variability in the patient's response after intervention. We argue that this variability could be reduced by the use of good anatomical and computational models that supply information on the part of the systems that we cannot directly observe.

The aim of the HEAR-EU project is to minimize invasiveness and insertion-induced trauma, and to improve the functional outcome of the implantation through the creation of patient-specific high-definition anatomical and functional models of the inner ear. Among the main objectives we would like to underline: a) the development of a novel high-resolution high-energy microCT device to obtain detailed images of the middle and inner ear, even in the presence of metallic implants, b) to build a model of the shape variability of the middle and inner ear from high-resolution images, also incorporating functional information, c) to build a computer-assisted patient-specific preoperative planning system d) to improve the design of cochlear implant (CI) electrode arrays and associated insertion tools using a population-based optimization framework.

Those objectives were fully reached during the course of the project, producing several important publications and exploitable results. We first concentrated on obtaining and analyzing high quality images that are used to build anatomical models (WP2). Then we provided highly detailed models of the inner ear, both on the anatomical and functional aspects. Later, we built predictive methods to estimate the precise shape of a patient's inner ear from standard low resolution CT images (WP3). Further, in work package 4, we developed a software platform for pre- and intra-operative planning. The system allows the assessment of not only the anatomy and structures of risk, but also the possible functional outcomes of the intervention. In order to validate the final position of the implant after the surgery we developed a novel high-resolution high-energy microCT imaging system in WP5. That allows to capture accurate images of samples in the presence of metallic devices such as the cochlear implants. Finally, in WP6 we devised techniques to improve the design of current CI electrode arrays and associated insertion tools based on a population-based implant design paradigm. The statistical shape models developed in WP3 formed the basis of a computational optimization scheme that maximizes the efficacy of the electrode array on a per-patient basis.

The scientific and technological advances produced during the execution of the project have been thoroughly disseminated and their exploitation is currently ongoing by the partners of the consortium. These results will significantly improve patient's quality of life until older age. Furthermore, they will also improve life expectations and performance for very young children allowing for even more efficient CI implantation at a very early age. Secondly, we will reduce hospitalization and surgery times required by CI surgery by making available the computerized surgical planning and diagnostic tools developed within this project. Importantly, improved functionality of CI will reduce battery consumption, again significantly lowering the running costs of this medical device. Moreover, HEAR-EU contributes to promoting the position of European industry in the EU and worldwide market of products and services associated to medical technologies.

Overall, the project has produced very important advances both theoretically and technically and the consortium is proud of what has been achieved so far.

Summary description of the project context and the main objectives (max 4 pages)

Cochlear implantation is a surgical procedure that aims to overcome hearing loss by direct electrical stimulation of the spiral ganglion cells in the inner ear. Technological progress in this area led to the development of implantable devices, which proved to be of great benefit to patients suffering from moderate to severe hearing loss.

The surgical scenario of implantation surgery is very complex. It requires high clinical expertise in order to 1) efficiently access the surgical site, the cochlea, localize nearby critical structures (e.g. facial nerve) and 2) optimize the position of the implantable device (electrode array) inside the cochlea. Furthermore, there is vast anatomical variability across patients and this makes individual optimal fitting an extremely difficult task. This also strongly influences the success of the surgery and the degree of hearing restoration. For example, within current surgical approaches it is not possible to estimate a priori the length of the cochlear duct of a patient, which varies between 25 and 35 mm. Such 30% variability in the population means that there might be a serious mismatch between the cochlear and implant frequency maps. This may lead to a confused pitch perception, reducing the benefit that could be obtained from the cochlear implant. Moreover, insertion trauma is of great concern in cochlear implantation. Hence, it is crucial that anatomical variability is considered not only during the surgical planning process, but also in the design phase of implants, in order to optimize functional outcome and reduce intracochlear damage and misplaced electrodes.

We hypothesize that a comprehensive understanding of the shape variability of the middle and inner ear among patients will be of assistance during surgical planning, and enable the design of improved hearing implants. Consequently, the aim of this project is:

1) to develop a novel high-resolution high-energy microCT device to obtain detailed images of the middle and inner ear, even in the presence of metallic implants,

2) to build a model of the shape variability of the middle and inner ear from high-resolution images, also incorporating functional information,

3) to build a computer-assisted patient-specific preoperative planning system

4) to improve the design of cochlear implant (CI) electrode arrays and associated insertion tools using a population-based optimization framework.

All objectives revolve around the criteria of minimizing invasiveness, insertion-induced trauma and enhanced functional outcome through patient-specific frequency mapping. Furthermore, due to the complexity of the surgical procedure novel technologies such as computer assisted planning could greatly benefit the training of young surgeons.

The research is based on the development of a statistical shape and functional model of the middle and inner ear, built from high-resolution cadaver microCT images. Novel high-energy microCT devices will be designed and developed. The statistical model will encapsulate the entire shape variability found in a given target population. Current techniques such as Active Shape Models (ASM) will be extended to perform automatically, on patient computer tomography (CT) and Digital Volume Tomography (DVT) scans, segmentation of the middle and inner ear, annotation of critical nearby structures of relevance for the surgical procedure, and patient-specific frequency-position mapping. This extension will be made possible by including during the modelling phase specific anatomical information (i.e. anatomical landmarks) and clinical expertise (i.e. surgical procedure), and frequency-position mapping (e.g. Greenwood functions). Additionally, the developed model will be used to optimize the design of future generations of CI electrode arrays by considering these spatio-functional and surgical requirements.

In the following we detail the objectives of the project per work package:

- The main objectives of WP1 are centered around translating the clinical requirements of the cochlear implantation procedure into detailed technical specifications for the system components to be developed. A milestone (MS1) will be reached once the clinical and technical details are clarified and the proper documentation is produced (D1.1).
- In WP2 we concentrate on obtaining and analyzing high quality images that are used to build anatomical models: acquiring the images of cadaver specimens in high resolution

using micro-CT technology and designing and implementing image analysis software to identify and delineate structures of interest (segmentation) and to align pairs of images from different acquisition times or modalities for data fusion (registration). Two milestones (MS2 and MS3) will be reached once a demonstrator and report of image analysis software is available (D2.1), a parametric model of implant design is defined and documented (D6.1) and all high-resolution cadaver data are acquired, processed and documented (D2.2).

- The next package, WP3, aims at providing highly detailed models of the inner ear, both on the anatomical and on the functional aspect. Its objectives are: to develop a statistical shape model of the cochlea and surrounding structures, incorporate functional information, such as cochlear frequency maps, into the statistical model. In addition, we will build predictive methods to estimate the precise shape of a patient's inner ear from standard low resolution CT images. To this end, a model of the modular transfer function describing the relationship between micro-CT and clinical CT will be built. Moreover, we will evaluate the predictive ability of the statistical shape model using clinical CT scans, with special emphasis on the critical structures and accuracy of the frequency map.

- Work package 4 develops a software platform for pre- and intra-operative planning, based on patient-specific models and providing decision support concerning the operability of patients, the implantation strategy and support of the pre- and intra-operative stage using appropriate visualizations. The system will allow the assessment of not only the anatomy and structures of risk, but also the possible functional outcome of the intervention. The software will be developed and designed to fit in the clinical workflow defined in WP1. The development process will be performed in close collaboration with the clinical partners at UBERN, who will participate in the validation of the system. It's milestone, MS4, will be reached once statistical model of shape and function are created and evaluated and the demonstrator is ready (D3.1). Additionally, as the cadaver images will be scanned with the new high-energy microCT system developed by WP5, there is a dependency on D5.1.

- The development of a novel high-resolution high-energy microCT imaging system is the main objective of WP5. That would allow to capture accurate images of samples in the presence of metallic devices such as the cochlear implants. Additionally, the design and implementation of a novel software and hardware infrastructure for efficient reconstruction and pre-processing of very large image datasets will be tackled by this workpackage. Eventually, the last task is the evaluation and optimization of the high-energy microCT system to be used in the validation of the cochlear electrode optimization work of WP6. In order to complete the work and reach MS5, we will first need the complete surgical planning system constructed and tested (D4.1).

- WP6 - The main objective of this WP is to improve the design of current CI electrode arrays and associated insertion tools based on a population-based implant design paradigm. The statistical shape models developed in WP3 will form the basis of a computational optimization scheme that aims at maximizing the quality of fitting of the electrode array to the modelled population while subject to constraints derived by the surgical and functional requirements defined in WP1. The optimization framework will be generic and applicable to other types of implants and medical devices in general. This work will be considered finished and MS6 reached after the final system demonstrators is ready and evaluated (D4.2, D5.2), the implant optimization studies are finished (D6.3) and generally all milestones are achieved and the deliverables completed.

- All the management tasks are grouped in WP7, to provide the overall strategy and coordination to the project, the steering efforts of the partners for the achievement of milestones and ensuring that the work is undertaken with appropriate quality levels. Also we aim to set-up a project management structure that ensures an efficient operational management including administrative, financial and legal issues, supporting the Scientific Coordination in organizing and supervising the pilot work and in its liaison with the European Commission. Finally, we will strive here to support the appropriate

communication and work dynamics to help drive the whole Consortium as a team towards successful completion.

- In WP8 we concentrate all the dissemination and exploitation efforts of the projects. We design a plan that allows for optimal communication within the project and the dissemination of information and knowledge generated by the project to relevant stakeholders. Also we disseminate the project knowledge and results to the research, clinical communities, as well as to the industry, the general public and patients. Finally, we develop an exploitation plan aiming at ensuring the use of the project results after the EC funding period.

Description of the main S & T results/foregrounds (max 25 pages)

By its completion at month 36, the project has successfully completed all its objectives and generated a number of important results. A summary of the main results of the different work packages is listed below:

WP1: Clinical requirements and technical system specifications

A comprehensive documentation of the most common hearing disorders, treatment approaches for cochlear implantation, and the state of the art of related surgical procedures was compiled. Clinical workflows were formalized and translated into technical specifications for the computer-assisted surgical planning system, the new high-energy microCT imaging system, and the design parameters for new cochlear implant electrode arrays.

The main results per task are:

T1.1 **Clinical requirements -** A literature research was performed to document the prevalence and incidence of the most common hearing disorders, treatment approaches for cochlear implantation, and the state of the art of related surgical procedures. Special attention was given to the benefits and risks of minimally invasive and robotic procedures. Clinical workflows were specified. This work was documented in deliverable D1.1

T1.2 - Technical system specifications - Technical requirements and guidelines were documented in D1.1, in relation to the design and development of the computer-assisted surgical planning system, the new high-energy microCT imaging system, and the design parameters for new cochlear implant electrode arrays. Functional system diagrams were provided for the software elements to be developed.

Brief summary of the results

In this section we resume the main results of the work package. Additional information is available in D1,1 and in the First Periodic Report.

Vision of a minimally invasive clinical workflow
In this section we provide a formal description of the current surgical procedure, including all critical stages and with special attention to the safety of associated risk structures.
Direct Cochlear Access (DCA) approach
Advancements in image-guided surgical technologies are now making minimally invasive surgery in the mastoid possible (Figure 1).
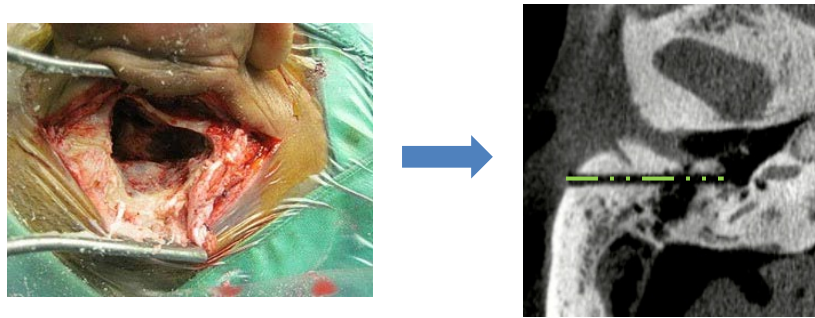
Figure 1: Reduction of co-morbidity can be achieved through minimally invasive surgical techniques. (Left) Traditional mastoidectomy created in the temporal bone directly posterior to the ear. (Right) CT slice coinciding with minimally invasive tunnel to the cochlea in a cadaver preparation.

The clinical workflow begins with the insertion of bone anchored fiducial markers (screws) into the mastoid region. A computed tomography (CT) image of the mastoid region with the fiducial screws in place is then obtained. From this data, an insertion trajectory is calculated and a drill guide with anchor points matching the fiducial marker locations is produced. After sterilization, the template is affixed to the bone anchored screws, the drill is mounted, and a key-hole tunnel is drilled to the cochlea. The final step of the procedure is the insertion of the electrode array into the cochlea and anchoring of the receiver unit on the skull surface.

WP2: High resolution imaging & image processing tools

High-resolution image acquisition and processing of 44 cadaveric samples was realised, in what consists one of the largest image databases of its kind. Algorithms and software for image processing were developed and applied to these datasets. Specific methodological developments include novel image segmentation protocols and tools for CBCT and microCT data, as well as image registration methods based on surface matching with Markov Random Field regularisation, and novel algorithms for implicit registration via partial differential equations.

The main results grouped by task are:
T2.1 - High-resolution image acquisition and processing Several samples were prepared and scanned: 22 dry temporal bones - µCT (16-19 µm) 16 Thiel-fixed cochleae - both µCT (7.6 µm) and CBCT (150 µm) 6 fresh frozen cochleae - µCT (5.8-10.8 µm) 8 of the Thiel-fixed samples were rescanned because of the presence of liquid inside.
An improved µCT reconstruction algorithm was developed by SCANCO specifically to process the dataset of this study.

T2.2 – **Segmentation -** A literature review of the state of the art in cochlear segmentation was carried out. We devised separate strategies depending on the image modality (µCT or CBCT) and on the fixation technique (Thiel and dry). **CBCT data** were segmented using region growing, Otsu thresholding and level set methods **Thiel-fixed data** were semi-automatically segmented using a variety of tools (Seg3D, ITK-Snap, Amira). **Dry data** were segmented similarly to the previous case, but the basilar membrane and the lamina spiralis were not visible in those samples due to the fixation protocol and were thus not segmented.

T2.3 – **Registration -** We worked on 4 different types of alignment. The first one is the **CBCT to CBCT** registration. This is to create a statistical shape model of the overall cochlear anatomy at clinical resolution. The second method was devised to perform **µCT to µCT** registration and its purpose is to build the statistical shape model of the data at the highest available resolution. The third method was **implicit registration** via parameterization, a very promising method using partial differential equations to put in correspondence the coordinates without actually performing the registration. The last

method was the creation of an **atlas of dry μCT**, to be used to segment new dry or clinical images.

Brief summary of the results

This section summarizes the work done to address the tasks T2.1-3. A detailed description of the results of T2.1 and T2.2 can be found in deliverable D2.2 that was filed by M18. A detailed explication of the work done to address the task T2.3 can be found in deliverable D2.1 that was filed by M12.

High-resolution image acquisition and processing

Different sets of cochleae have been scanned at different levels of resolution with micro-computed tomography (microCT) by SCANCO and clinical cone beam computed tomography (CBCT or DVT) by UBERN.

Table 1 summarizes the number of specimens that have been scanned

Specimens	*Source*	*Number*	*MicroCTScans*	*CBCT Scans*
Dry temporal bones	Anatomical collection of the University of Bern	22	15 @ 16.3 μm 5 @ 19.5 μm	0
Thielfixedcochlea	Donorprogram	16	16 @ 7.6 μm	15 @ 150 μm
Thiel fixed cochlea after drying procedure	Same specimens as the Thiel fixed cochlear bones	8	8 @ 11.4 μm	0
Fresh frozen cochlea	From Prof.Dr. Starks work published in [7]	6	2 @ 10.8 μm 3 @ 5.9 μm 1 @ 5.8 μm	0

Table 1: List of all measured specimens used in the HEAR-EU Project.

T2.2 Segmentation
This section summarizes the work done to address the task T2.2. A detailed description can be found in deliverable D2.1 that was filed by M12. The work has been monitored and coordinated by ALMA and processed by ALMA, DTU and UBERN.

Segmentation of microCT data
The strategy and goal for the segmentation of microCT data depends on the type of fixation/specimen processing, image quality, etc. Although the tools and approaches for various datasets are similar it makes the most sense to describe the segmentation of Thiel-fixed and dried specimens separately.
The fully processed dataset was segmented by several project partners (ALMA, UBERN, DTU). This was done to establish a common understanding of the anatomy and segmentation, and to see how similar the segmentations would be. A description of the segmentation protocols can be found in D2.1.

Dry specimen segmentation:
The data contain the 'macroscopic' structures of the inner ear (i.e. cochlear, vestibule and semicircular canals) and the parts of the surrounding. The contrast in the images allows a distinction between bone and non-bone structures. The data was therefore segmented using a single object/label representing different anatomical location (see Figure 2)
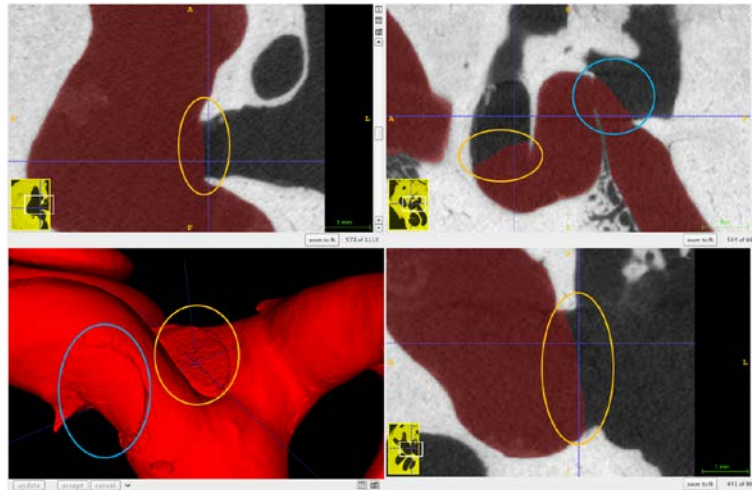
Figure 2: The dry specimen segmentation at oval (yellow) and round window (blue) niches

Registration of CBCT to CBCT

This section describes the work done regarding a registration of 9 CBCT/DVT clinical datasets provided by the university hospital in Bern. The goal of this registration is to provide the data needed for building a statistical shape model of the gross cochlear anatomy (see T3.1) to be used in relation to other tasks. The approach for the registration was a group-wise registration using the Elastix software.

Group-wise registration: The group registration was performed. The program calculates a deformation of each individual dataset to obtain an estimate of the 'true' mean dataset. A manual segmentation of the cochlear in the mean image could then be made. The inverse deformation, i.e. the deformation of the mean image to each of the original datasets, could be found using Elastix. The deformation was applied to the surface model extracted from the mean segmentation as well (see T3.1), thus providing 7 registered cochlear surface models with point correspondences.
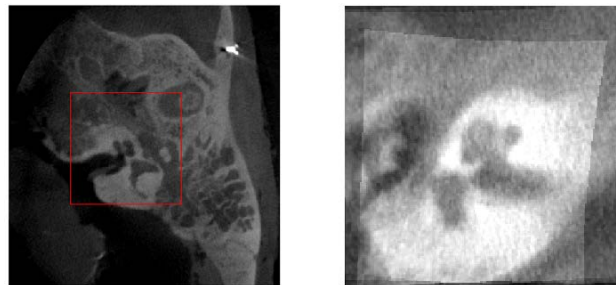
Figure 3: (Left) Showing the cube region cut out of a CBCT image as part of the data preprocessing. (Right) Showing a slice of the mean image volume obtained from a group-wise registration

Registration of µCT to µCT

This section describes the work done regarding a registration of the dried µCT data (see T2.1 and T2.2) with the purpose of building a statistical shape model of the anatomy represented in the data.

The approach for the registration has been to select a reference dataset/shape that is thought to be similar to an unknown mean shape. All other individual datasets should then be registered to the reference.

Initial registration: The initial position and orientation of the data is initially quite varying. It is therefore reasonable to do an initial rigid registration to place all the data in a common position and orientation (see Figure 4).
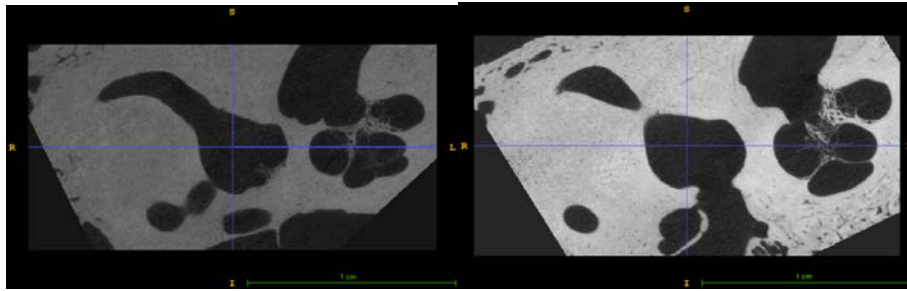
Figure 4: The center slice (xz-plane see Figure above) of two datasets after initial alignment (the cursor points to the origin of the global coordinate system)

Deformable registration: The initial alignment is followed by a deformable registration between the reference and each individual shape. The anatomy of inner ear/cochlear is inherently a challenging shape to register and requires that the framework has several features and options.

The best results were achieved with a registration of the binary segmentation volumes (see Figure 5). Adding a landmark at the apex could provide a better fit of the apex, but only in datasets that were not too dissimilar to the reference.
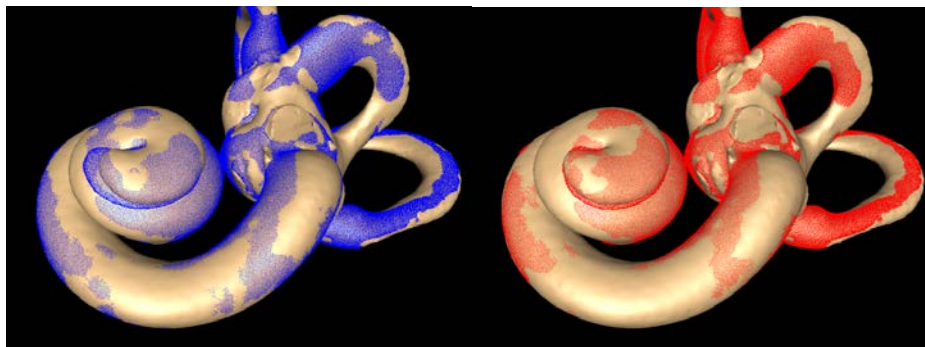
Figure 5: Brown/yellow surface is the target surface. The blue and red shape respectively shows the result of deformable registration without and with an apex landmark

Atlas of dried microCT

Semi-automatic segmentations performed on the Dry datasets, were used to build a probabilistic atlas image. One of the images was selected as reference image. The rest of the segmented images were registered using Elastix software. Affine registration was used to put all the images in correspondence with the reference image. After registration, the same transformation was applied to each of the corresponding segmented binary images. The same transformation was used for the round window and oval window images. Once all the transformations were applied to the binary masks, a series of grey level images were generated with the probability of each voxel to belong to the cochlea (plus vestibuli and semicircular canals) and windows. The atlas will be employed as a means to segment new dry or low-resolution images.

WP3: Statistical models of inner ear shape and function

Statistical Shape Models (SSMs) have been built from both clinical CBCT scans and high-resolution microCT data. These SSMs describe in a compact manner the shape of the inner ear and the variations found in the population. A framework for patient-specific shape estimation by instantiating this model from imaging data was completed. Further, functional simulation has been incorporated into the models via Finite Element Models, to perform advanced mechanical and electrical simulations of cochlear and implant function. The software and model have been distributed for use in WP4 and WP6, from where the usability and potential are explored further.

The main results grouped by task are:

T3.1 - **Statistical shape model -** A pipeline to transform the segmented datasets from WP2 into a statistical shape model was created. Two statistical shape models were created, one using clinical CBCT data and the other one using microCT. In the **clinical** one**,** the point distribution model was used to create the SSM from 7 samples. The purpose of this initial model was to provide realistic deformation fields to other tasks, especially for the Finite Element Model (T3.3). The **microCT-based** statistical shape is built using the Statismo software and used to generate shapes corresponding to the first and second modes of variations. The first mode describes variations in the length of the cochlea, while the second mode describes variations in the width of the basal turn.

T3.2 - **Patient-specific shape estimation -** The shape model has been updated and finalized along with a software package for fitting the model to clinical CT images. A validation study has been performed as part of WP4. The software and model have been distributed for use in WP4 and WP6, from where the usability and potential are further explored.

T3.3 - **Enrich the statistical model with functional info -** This task was started ahead of planned schedule and both Alma and UPF joined this task. We created several versions of a finite element model to simulate the tonotopic properties of the cochlea. Additionally, we created an electrical model that captures the main characteristics of the stimulation of deeply implanted cochlea. The current model incorporates both mechanical and electrical simulations.

T3.4 - **Functional predictive analysis -** We annotated the SSM with the frequency mapping around both the spiral ganglia and the organ of Corti. We were thus able to propagate this information to both real and virtual patients. The predictions have been validated against literature.

Brief summary of the work

In this section we briefly summarize the main results. The procedures for making patient specific estimation of the inner ear shape from clinical CT images were finished by month 24 of the project. An initial description and evaluation was included in D3.1. The fitting procedure was detailed additionally in D4.1.

From volumetric segmentation to surface model:
This section describes the pipeline that has been set-up to obtain surface meshes from the segmented datasets. There are several advantages in building and working with statistical shape models as surface models rather than trying to keep the data as volumetric images.

Model building using high-resolution data:
A shape model of the inner ear based on the dried µCT data has been built. More data and improvements are planned to be added to the model. No shape modelling has yet been attempted on the thiel-fixed µCT data. The limited amount of data and the difficulty in obtaining the desired segmentations have postponed this branch of the shape model building process.

The inner ear model based on dried specimens:
The dried µCT data show none of the soft-tissue structures. However, the overall shape of the entire inner ear can be well described using a single surface. The model should fit well into the other WP tasks, and will serve as a good starting and reference point for other model building activities.

Establishing point correspondences: After the image registration steps (T2.3) of the dried µCT datasets the corresponding surface models of the inner ear still contain a varying number of vertices and triangles. In order to build the statistical model a point-to-point correspondence has to be found between the reference shape and each individual shape. This could essentially be considered an extra step in the registration procedure of task T2.3, except that is doesn't involve any geometric transformations, but rather a re-ordering/re-meshing of a surface model.

Building a statistical shape model: The point-matched surface shapes have been built into a point distribution statistical model using the Statismo library. The model described here (see Figure 6) was based on 6 shapes.
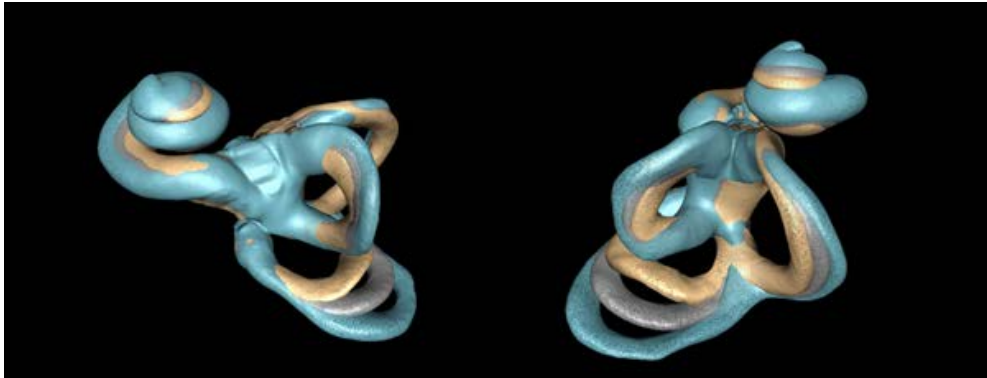
Figure 6: The shape model variability of the first mode. The mean shape (mean) and +/-3 standard deviations (blue and yellow respectively) are shown

The modes of variation in the shape model capture several things. Given that the apex registration is not ideal and the low number of samples some of the observed variability might change as these issues are dealt with.

Patient specific estimation of the inner ear shape

The software package for this procedure has since then been finalized and distributed to be included in the surgical planner software.

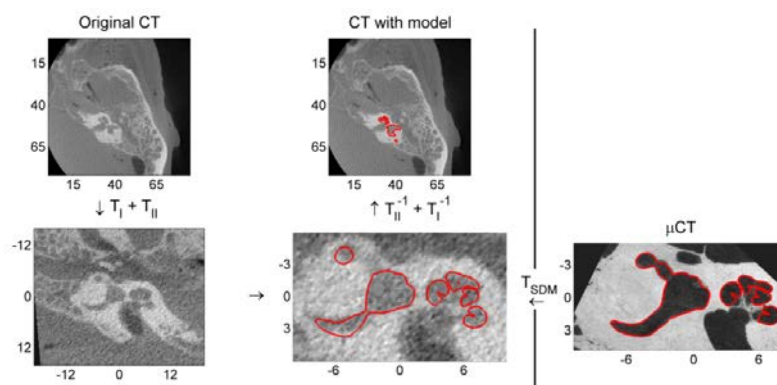Figure 7 recaps the steps of the final proposed procedure.

Figure 7: The steps of the fitting procedure. A landmark-based initialization (T_I) is calculated (see also Section 4.1.2) and followed by a rigid image registration (T_II). This brings the CT data into the space and position of the trained Statistical Deformation Model and the reference micro-CT dataset. A non-rigid registration (T_SDM) regularized by the SDM is performed and the predicted anatomical shape is projected back to the original CT image.

The Statistical Shape Model was updated with a new underlying registration model driving the shape variability, and with a new reference dataset in order to incorporate an estimate of

an additional important intra-cochlear structure – the cochlear partition (equivalent to the basilar membrane). This new model and the fitting procedure were included in a small validation study. This study was detailed in D4.2, and a qualitative evaluation of the accuracy and result can be seen in Figure 8.
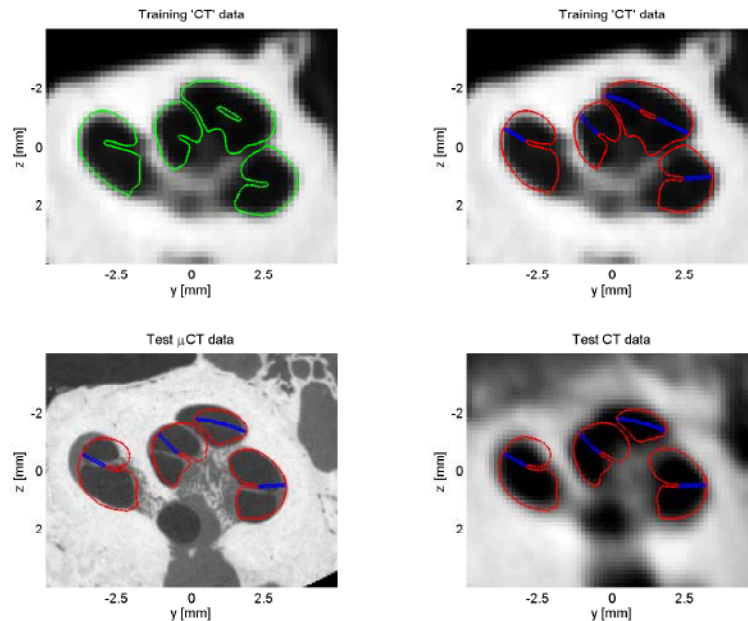

Figure 8: The visual accuracy of patient specific shape estimation. Top row: The model was fitted to a CT-version of a training micro-CT dataset (top right), and compared against the ground truth segmentation (top left). Bottom row: The model was fitted to a test data CT image (bottom right), and further overlaid to the corresponding thiel-fixed micro-CT dataset for evaluation of the accuracy.

Cochlear FEM modelling and functional predictive analysis

In this task, we annotated the mean shape of the SSM with the frequency mapping and we were thus able to use the same framework to propagate both the anatomical and the functional information to new clinical scans. In addition, we performed an initial validation of the predictive analysis, compared with existing literature, and validation with electrophysiological data was initiated, as explained in detail in WP4.

A framework for automatic patient-specific finite element model generation was developed. The first step in the framework is to use the SSM and the patient's clinical CBCT scan to obtain the high-resolution mesh that best describes this patient's geometry, as shown in Figure 9.
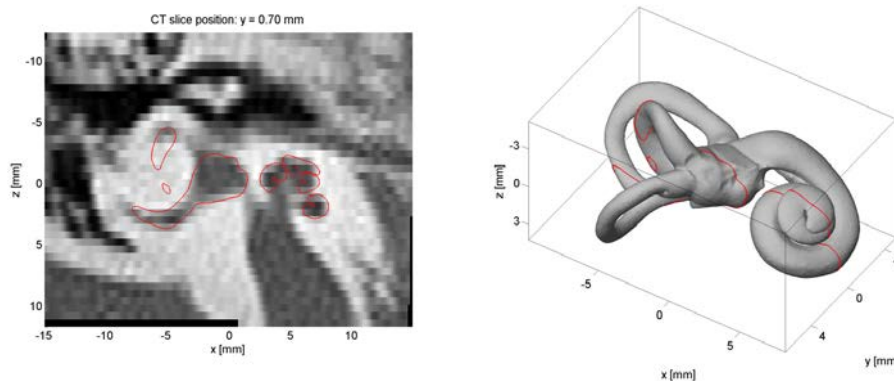
Figure 9: Fit of the SSM to a clinical case with CBCT. (left) We see the original CBCT data of the patient and, in red, the information recovered with the SSM. (right) We see the best fit of the SSM for this patient and in red the plane used for visualization in the image on the left.

Then we use the CAD design from the implant manufacturer and the trajectory of the simulated insertion to position the desired implant inside the model of the cochlea. Once the surface mesh of the whole hearing model is created, including the cochlea, electrode and surrounding bone, we proceed with the volumetric mesh generation. All independent meshes were merged automatically, ensuring the lack of intersection. In order to ensure the convergence in the subsequent finite element electrical simulations, the mesh quality was assessed. Nerve fibres were added to the model, to be able to couple electrical stimulation and neural response. An automatic method was developed for the generation of the nerve fibres along the patient-specific cochlea. For the cochlear implant simulation, we modelled a monopolar stimulation protocol, where each electrode is activated and stimulates with an intensity of 1mA, and the surrounding bone acts as a reference. The protocol was implemented in a template simulation using the quasi-static electrical regime of the Maxwell equations as implemented in the Elmer multiphysics solver. The boundary conditions were defined only once in the template of the SSM and then propagated to all the instances of virtual patients created by sampling the SSM.

This enables our approach to potentially scale to thousands of patients because no manual intervention is required.

Once the model is ready, we simulate the effect of the given surgical planning. This is a very powerful technique that provides important information about what is happening in the patient's anatomy. As shown in
Figure 10 and Figure 11, the activation of each electrode causes a very different voltage distribution. In this case, the most basal electrodes show some degree of selectivity, while the apical ones cause a lot of noise and cross-activation of different nerves. This suggests that the patient could benefit from a different programming or a reduction in the activity in those apical electrodes.

Validation of the monopolar case
As initial validation of the electrical simulation, we compared the results obtained by our model with the monopolar stimulation protocol to the ones presented in literature. In this work, the author measured the impedance along the spiral ganglion path produced by the stimulation of 22 electrodes activated separately in a synthetic model

The comparison has two main steps: first we compare the value of the impedance measured by each electrode, and then we compare the sensitivity of our results with respect to the changes in the electrical properties of the components of the model.

In the first part we generate an excitation spread curve, as shown in Figure 12, where we record the impedance measured along the spiral ganglion per each electrode activation and compare with a similar results in literature

The comparison of the results shows that the same important features are maintained. Nevertheless, perfect correspondence is not achieved, as the geometry of the model is different and the amount and disposition of electrodes is different.
Globally, our simulations give results similar to literature, as the main important features are reproduced.
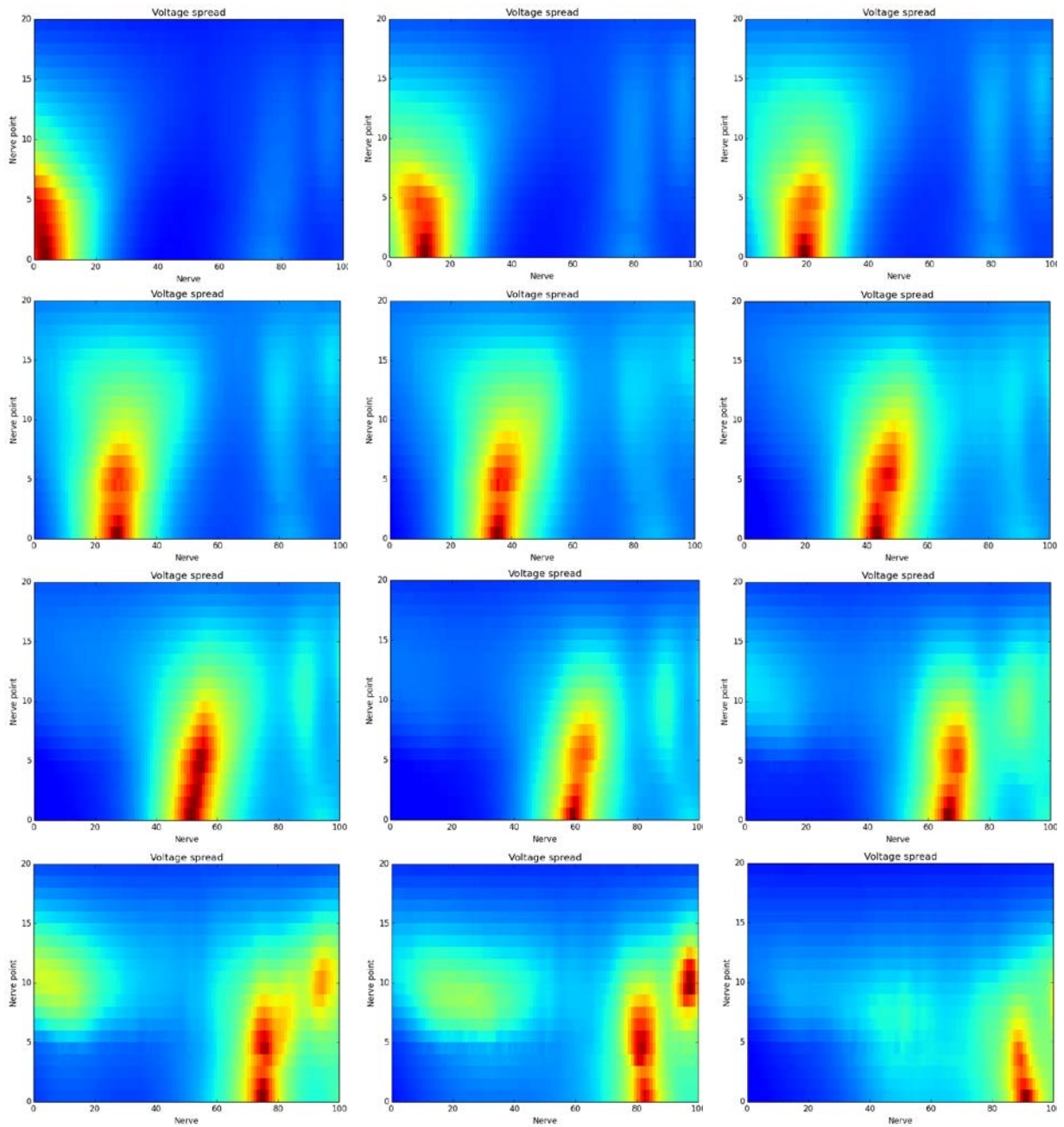
Figure 10: Spatial activation maps, showing the results of the simulated electrical activation for the given surgical plan. Each plot, from left to right, top-down, shows the effect of the activation of one electrode, from the most basal to the most apical one. In each image the horizontal axis is the interested nerve, oriented tonotopically from basal to apical and the vertical axis the compartment of each nerve.
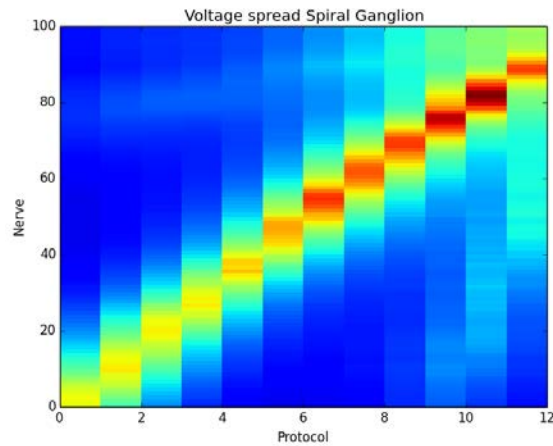
Figure 11: Full voltage spread measured at the spiral ganglion. We summarize in this figure the extended simulation results shown in the previous Figure. A perfectly selective stimulation should result in a straight diagonal, with very local excitation. Excitation far from the diagonal represents cross-talk stimulation that we want to reduce.

(a)   *(b)*
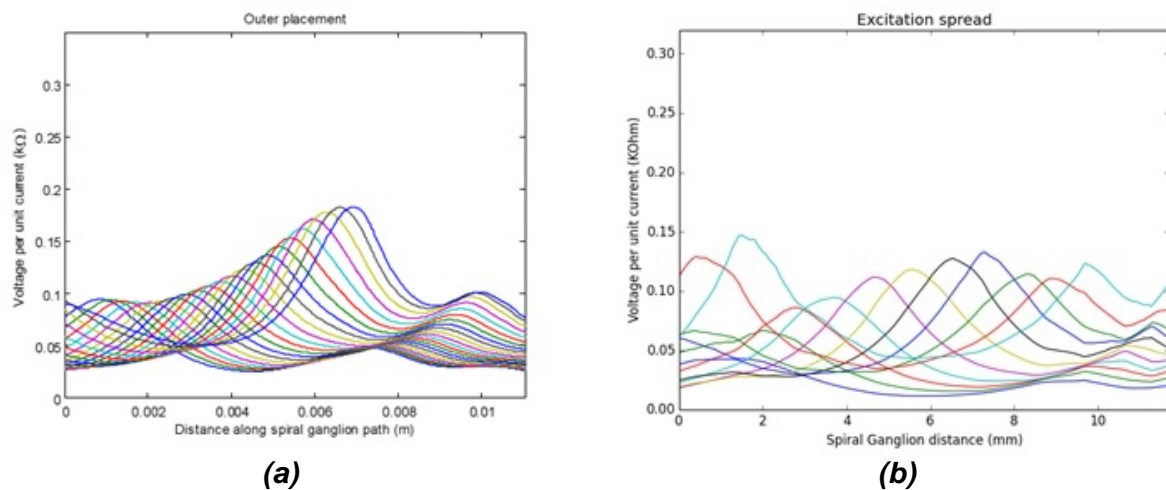
Figure 12: Comparison of the results obtained in literature(left) and our model (right). The horizontal axis shows the distance along the spiral ganglion and the vertical axis the impedance measured. Each color corresponds to a different activated electrode.

WP4: Computer-assisted surgical planning system

A system for the CI surgical planning has been developed. The system includes the planning of patient-specific middle ear anatomy from CT/CBCT, the selection of a safe drilling trajectory to the cochlea, the definition of finer intracochlear anatomy using a statistical shape model built from microCT data and the optimization of the electrode array insertion angle for atraumatic implantation. The system is able to define safety regions to avoid critical anatomy while drilling the access to the cochlea and to use the statistical shape model of WP3 to generate customized cochlear models. Validation of all different components, as well as the integrated surgical planning system was performed.

The main results grouped by tasks are:

T4.1 - **Planning system: design, development and testing -** A system for CI surgical planning has been developed. The system includes the planning of patient-specific middle ear anatomy from CT/CBCT, the selection of a safe drilling trajectory to the cochlea, the

definition of finer intracochlear anatomy using a statistical shape model built from microCT data, and the optimization of the electrode array insertion angle for atraumatic implantation. Furthermore, it is able to simulate the implantation of different electrode models, insertion depths, stimulation protocols, etc., in order to plan the most appropriate implantation strategy.

T4.2 - **Patient-specific surgical plan -** The system is able to define safety regions to avoid critical anatomy during drilling the access to the cochlea and to use the statistical shape model produced by the output of WP3 to generate customized cochlear models.

T4.3 - **Evaluation of the surgical planning system -** Validation was performed for all different components individually, as well as the integrated surgical planning system.

Brief summary of the work
Additional details can be found in D4.1 and D4.2 filed by month 28 and 36 respectively.

Planning system design, development and testing

Surgical planning software description
Following the scheme outlined in the deliverable D4.1, the developed planning software system was conceived to render 3D models to aid in understanding the spatial relationship between anatomical structures of a specific patient. The workflow of the planning software system was designed to incorporate the knowledge and tools gathered in other work packages developed by all partners. In order to reduce dependences amongst partners and improve parallel work, the workflow has been divided into two main components are as follows:
- **Surgical access planning component:** to allow the modeling of the patient's ear anatomy and defining a suitable and safe drilling trajectory to access the cochlea;
- **Electrode insertion component:** selecting and positioning a suitable cochlear electrode array as well as simulating the insertion process.
  More details about the two components and validation works are provided in the next sections. Figure 3 provides an overview of the functionalities of the above components.
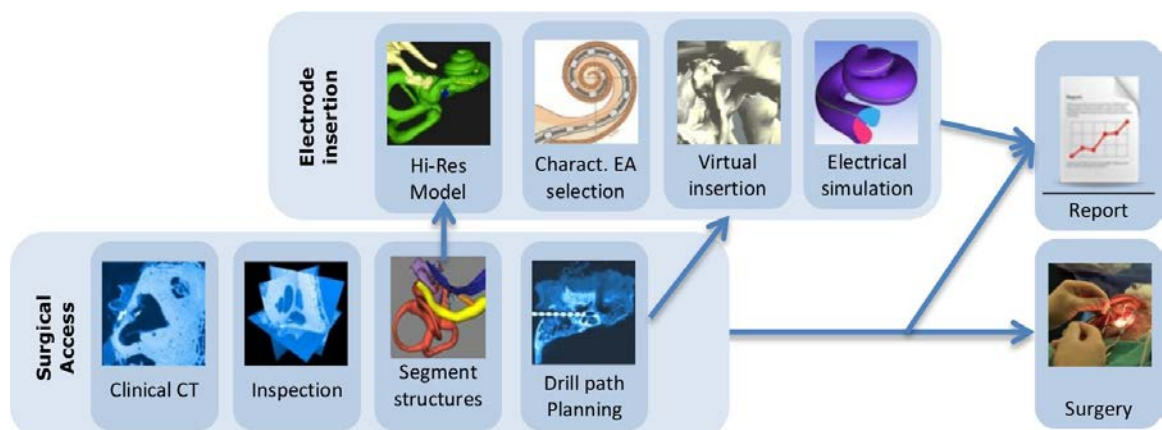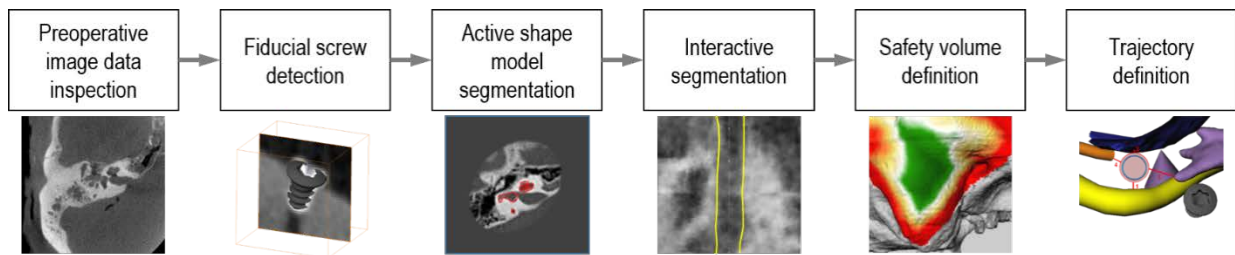

Figure 13–Design approach of the HEAR-EU surgical planning system consisting of specific software modules for surgical access planning as well as the planning and simulation of the electrode insertion.

Surgical access planning component
The following figure depicts the workflow of the surgical access planning component.

**Figure 14 – Workflow of the surgical access planning component.**

In brief, the workflow of the surgical access planning component is as follows:
1. Inspection of preoperative CT/CBCT images of the patient using multiplanar axial-coronal-sagittal visualization for diagnosis of anomalies such as malformations.
2. In case of image-guided surgical procedure, fiducial screws inserted into the patient prior to imaging are localized in the preoperative image for later patient-to-image registration.
3. Initialization for active shape model segmentation (WP3) is performed by placing four landmarks to define a reference system used by the subsequent planning component to segment the labyrinth.
4. Active shape model segmentation can be challenging for middle ear structures due to the inhomogeneity of the temporal bone. For this reason, the surgical access planning component provides semi-automatic segmentation approaches to all relevant structures of the ear: the mastoid, the posterior external auditory canal wall, the facial nerve, the chorda tympani, the ossicles (incus, malleus and stapes) and the labyrinth (containing the cochlea).
5. Safety zones are defined in order to plan a suitable drilling trajectory. Two main methods have been investigated in order to create and indicate safety volumes: geometric analysis of the bone thickness using topographic maps and computation of safety margins accounting for system errors.
6. In an iterative process, the trajectory is selected to avoid any critical anatomy while optimizing for an atraumatic insertion trajectory angle.
7. The plan is exported for later processing in the electrode insertion component. In addition, the software system can be used in conventional surgical procedure as a support for the surgeon or in image-guided cochlear implantation using a robotic device.
   A detailed description of the methodology for the different steps is presented in D4.1 and D4.2. Validation of the different components is presented in D4.2, and summarized hereafter.

**Feasibility of surgical planning for conventional cochlear implantation**
In addition to minimally invasive procedures it was hypothesized that, by reducing complexity and improving understanding, computer assisted preoperative planning may aid surgeons in the conduction of conventional hearing device implantation procedures in cases of malformation and in cases of normal anatomy. To investigate this hypothesis, the efficacy of the developed planning tool was validated by three surgeons for conventional cochlear implantation surgery, in a prospective single arm clinical pilot study.
Within a single institution (University Hospital, Inselspital Bern, Switzerland), computer assisted planning was employed in eight cochlear implantation procedures. No exclusion criteria were applied and thus, both cases with and without malformation were included. For each case, a plan was created from preoperative CT images by a technician together with a surgeon using the proposed planning software system. Anatomical structures including the mastoid, external auditory canal, facial nerve, chorda tympani, ossicles, sigmoid sinus wall, middle fossa dura and lateral semicircular canal were segmented(see Figure 15).
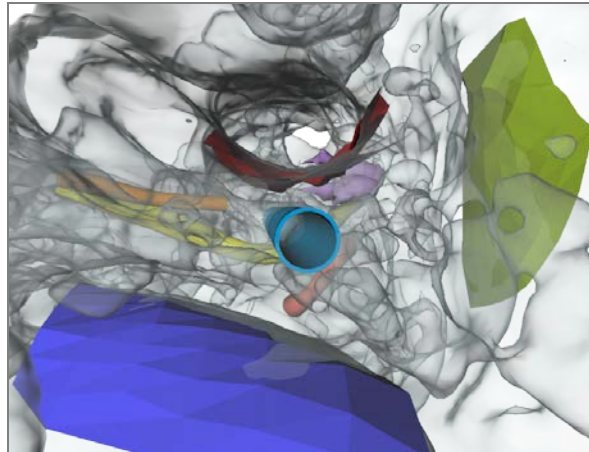
Figure 15 – Patient specific plan for a conventional cochlear implantation. Sigmoid sinus wall (dark blue), posterior tympanotomy (light blue tunnel), middle fossa dura (green), external auditory canal (dark red), ossicles (purple), lateral semicircular canal (pink), chorda tympani (orange), facial nerve (yellow).

Surgeons indicated that the plan predominantly aided in 3D understanding of the anatomy (54%) and in locating the facial nerve (62%). In the first three cases, the plan was reported to only "slightly" improve confidence during surgery while in the five later cases, surgeons reported that the plan improved their confidence on average "very much" (see Figure 16).
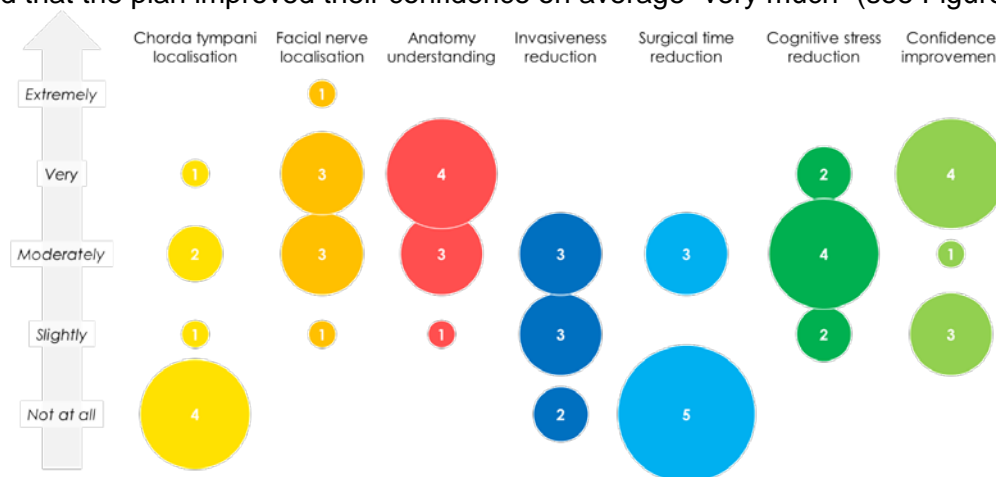

Figure 16 – Perceived assistance using the proposed preoperative planning system in N = 8 cochlear implantations.

This study presents an initial investigation into the efficacy of computer assisted preoperative planning for conventional cochlear implantation procedures.

Patient specific surgical plan

The EIM includes the fitting software for estimation of the high resolution, patient specific anatomy. This model is based on the SSM/SDM developed in WP3.

The high resolution enables cochlear characterization and EA selection step. The software provides information about commonly used insertion depth angles (Figure 17 left). Once we have an estimation of the CDL, we can—using the Greenwood function for the case of humans—estimate the depth vs. frequency map (Figure 17 right). The operator is suggested with a range of electrodes to insert, and can place the electrode contacts near the desired frequencies. The dialog includes a residual hearing indicator for visualization of this depth mark vs. the insertion depth.
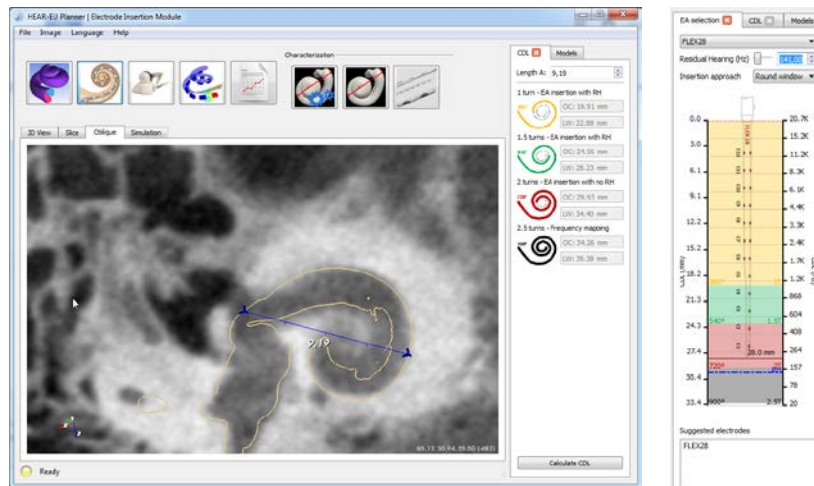
Figure 17: Estimation of the "A" distance, CDL, and insertion depths (left). Depth vs. frequency map with residual hearing and EA selection (right).

Once the operator selects a proper insertion depth for the patient, the software can enter the simulation phase. First, a virtual insertion is performed. The virtual insertion aims at virtually placing the electrode array at the expected depth for estimation of insertion risks and further electrical simulations. If the study includes DCA trajectory information, the selected trajectory is determined by the DCA data. Otherwise the virtual insertion uses the epsilon and delta angles to establish the insertion trajectory of the EA into the cochlea (Figure 18 left). A force selection wheel is used to specify the insertion force applied (Figure 18 right).
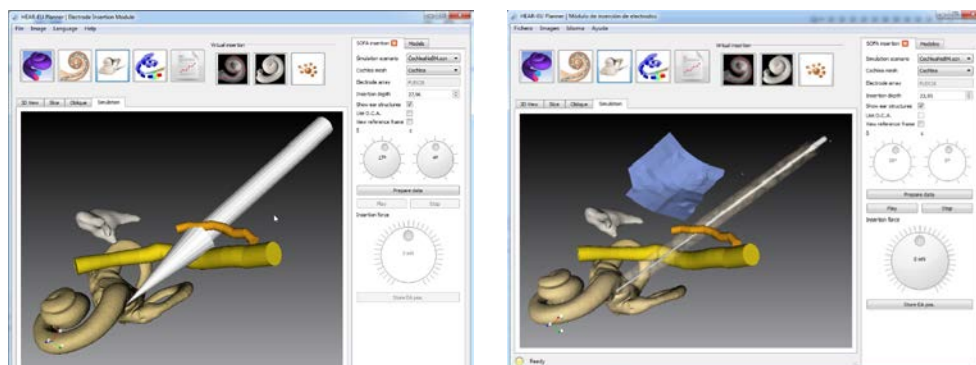
Figure 18: Selection of insertion trajectory (arrow) based on angles delta and epsilon (left). The arrow switches to the selected EA geometry, and the insertion can start (right).

Once the EA is virtually placed in its final position, the final positions of the electrode contacts inside the cochlea can be exported so they can be used to perform the electro-physiological simulation

WP5: High-energy micro-CT system

The new high-energy microCT scanner prototype is up and running. The hardware development was based on a previous model (ScancoµCT-100). A new X-ray source and a new scintillator/detector system have been integrated. This new system can now be operated at a peak energy of 130 kVp, at a spatial resolution of about 6 µm and with a field of view of 13 mm. A metal artefact reduction (MAR) reconstruction algorithm has been implemented for the optimal imaging of the electrode array implanted in the cochlea. This algorithm significantly removes artefacts and improves image quality around the implant array.

Figure 19: Prototype of the high-energy microCT system. The magnification shows the controller board that had to be developed for controlling the detector and for retrieving the acquired images. Some specification of the controller are given in the table.

A list of results grouped by tasks is below:

T5.1 - **High-energy hardware design, development and testing** The new high-energy microCT scanner prototype is running. The hardware development was based on a Scanco µCT 100, where a new X-ray source and a new scintillator/detector system was used. This new system can now be operated at a peak energy of 130 kVp at a spatial resolution of about 6 µm at a field of view of 13 mm.

T5.2 - **Optimized software and hardware for image reconstruction and pre-processing of very large datasets -** A metal artefact reduction (MAR) reconstruction algorithm has been implemented for the optimal imaging of electrode array implanted in cochlea. This algorithm significantly removes artefacts and improves image quality around the implant array.

Brief summary of the results

Additional details can be found in D5.1 and D5.2, filed by month 24 and 36 respectively.

High-energy hardware design, development and testing
In this work package, a new high-energy microCT system has been developed. The development strategy was to build a system that was based on the commercially available cabinet system µCT-100 to minimize the development uncertainties and to ensure that the system was ready for use in the HEAR-EU project. This new system includes hardware developments as well as algorithms to suppress metal artifacts caused by the electrode array.

The prototype of the new high-energy system was successfully designed, assembled and evaluated. It is equipped with a new X-ray source, a new scintillator/detector system as well as a new controller board to synchronize the detector for the measurement and to retrieve the acquired data. The prototype was finished in time and phantoms as well as real specimens have been measured. Figure 19 shows the new high energy microCT system running with the new controller board still outside the main housing.

It could be shown, that the new system is working at a peak energy of 130 kVp at a comparable resolution as the µCT 100. Although it was visually found that images of the new system were slightly sharper, the actual resolution determination using a cylinder phantom did not support this result. The reason for this was a more pronounced in-line phase shift as compared to µCT 100, as well as higher scattering due to the higher energy, yielding in an edge enhancement that limited the determination of the spatial resolution using the MTF

method. Therefore, a classic line-pair phantom was used and a similar resolution could be observed for the old and the new system (Figure 20).
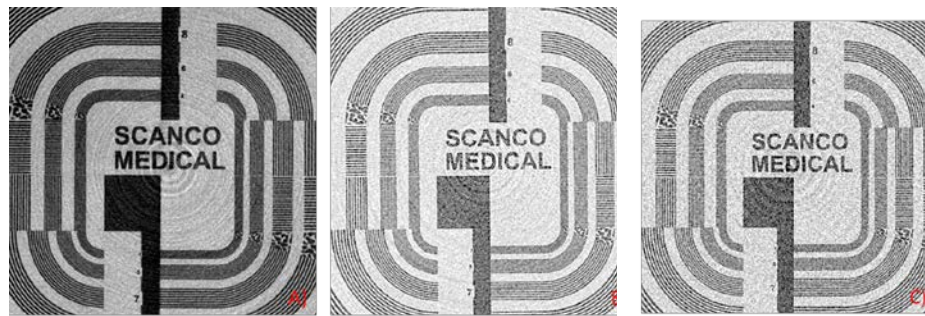
Figure 20: Magnification of resolution phantom. A) µCT-100 at 70 kVp voxel-size 1.6 µm, B) High-energy µCT-100 at 70 kVp voxel-size 1.7 µm, C) High-energy µCT-100 at 130 kVp voxel-size 1.7 µm. A further evaluation of the hardware showed a signal to noise ratio (SNR) that was about two times lower as compared to the µCT100. Thus, a longer integration time is required on the new system to get the same image quality. However, this is a minor issue that may be resolved in a follow-up version using a different scintillator.

Leakage radiation of the new system is equivalent to background noise and thus, the system can be considered to be a full protection device. The new system fits therefore well with the concept of the other cabinet systems of Scanco Medical.

Optimized software and hardware for image reconstruction and pre-processing of very large datasets

To remove artifacts, caused by the dense metal of the electrode array, the classic metal artifact reduction algorithm (MAR1) was implemented and compared to a normalized metal artifact reduction (NMAR) method. For this project, MAR1 resulted in better images and thus, this algorithm was chosen to correct the data of the HEAR-EU project.

Figure 21 shows the uncorrected and MAR1 corrected reconstruction of a cochlea with an electrode array inserted. It is obvious, that the bright streaks could be removed and that the electrode array is better confined. The close-ups further show, that the membrane is much better visible in the MAR1 corrected image. Thus, in this case, the correction worked fine and significantly improved the results.

Figure 22 shows the same sample as in Figure 22 but a few slices further down. Also in this case, the metal artifacts could well be removed. However, the basilar membrane is lost after MAR correction in the region pointed to by the yellow arrow. These two figures of the same sample illustrate the advantage as well as the limitation of MAR1 and in general MAR algorithms. The artifacts may well be suppressed and lost tissue structures may be recovered, however, it can also happen, that some tissue structures disappear in the corrected image. Thus, it is essential to carefully compare the corrected with the uncorrected reconstruction to get most out the data.

In conclusion, a new high-energy microCT system and software has been developed and evaluated and the system could be used to measure the specimens of the HEAR-EU project. The system still needs some issues to be resolved before it can be brought to market. A system with an energy of 130 kVp would be useful especially in studies involving implants as for instance the evaluation of dental implants in bone. Therefore, Scanco Medical is working hard on bringing this system to market in the very near future.
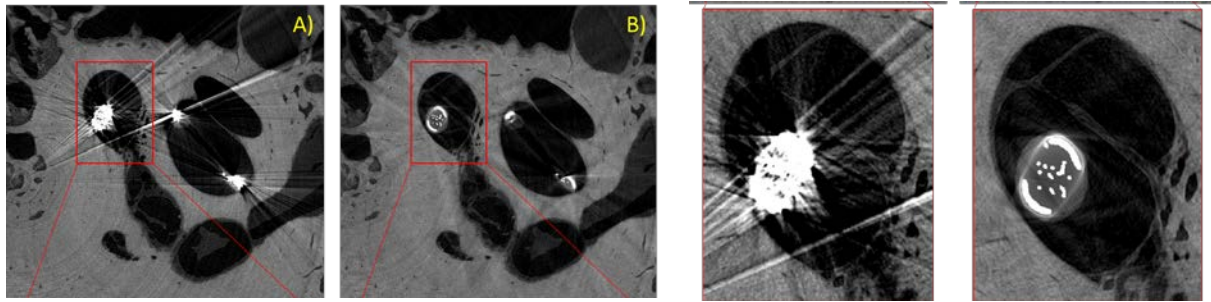
Figure 21: Metal artifact correction using MAR1. A) Uncorrected reconstruction, B) MAR1 corrected reconstruction.
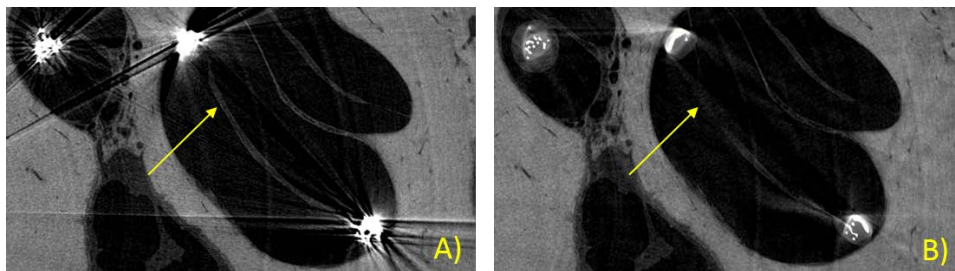
Figure 22: Metal artifact correction using MAR1. A) Uncorrected reconstruction, B) MAR1 corrected reconstruction. The arrows points to the lost membrane after correction.

WP6: Implant design optimization

A combination of metrics has been developed to evaluate the compliance of the array to the scala tympani size (likelihood of trauma) and the relative position between the electrodes to the stimulation targets (frequency coverage and specificity). Based on these metrics, an optimization framework was developed and applied to optimize CI implant designs. A prototype of electrode array with a new design, determined in T6.2, was manufactured. The new design was validated in a series of bench tests with plastic models of the human cochlea and cadaveric temporal bones. Furthermore, the insertion forces needed for a full insertion were also measured and compared to those for the Med-EL Flex28 electrode array. The results indicated that the new design should be as atraumatic as Flex28 itself. Subsequently, the novel high-energy microCT system, developed in WP5, was used to obtain high resolution microCT images of the implanted cadaveric cochlea with minimized metallic artefacts, to assess coupling efficiency, distance to the neural tissue, and insertion trauma. In total 4 cadaveric temporal bones were implanted. In addition to the CI electrode array development, several insertion tools were designed, constructed and tested, with the aim to assist surgeons with electrode insertion in anatomically difficult situations.

A brief summary of the results grouped by task is below:

T6.1 - **Framework for model-based global optimization -** The properties of the statistical shape model have been leveraged for generating a set of cochlea shapes and for automatically extract the structures of interest for frequency mapping and estimating the ideal tangential trajectory for a candidate electrode array of cochlear implant (CI).

T6.3 - **Evaluation / test case -** The prototype of electrode array with a new design determined in T6.2 was manufactured. The new design was validated in a series of bench tests with plastic models of the human cochlea and cadaveric temporal bones. The results indicated that the new design should be as atraumatic as Flex28 itself.

T6.4 - **Framework for model-based global optimization -** The properties of the statistical shape model have been leveraged for generating a set of cochlea shapes and for automatically extract the structures of interest for frequency mapping and estimating the ideal tangential trajectory for a candidate electrode array of cochlear implant (CI)

Statistical shape model for morphometry and implant position estimation

The statistical shape model (SSM) describes the anatomical variability as a multivariate normal distribution, and provides a compact parametric representation of the cochlea shape. This representation allows the generation of new shapes, which is at the base of the population based framework for the design optimization of the electrode array of cochlear implant (CI).

Thanks to the topology preserving properties of the SSM, the spiral curve corresponding to the lamina spiralis has been automatically delineated on each sample by propagating an initial set of landmarks picked on the mean cochlea shape. A principal component analysis was performed around those landmarks to estimate the radial direction (Figure 23
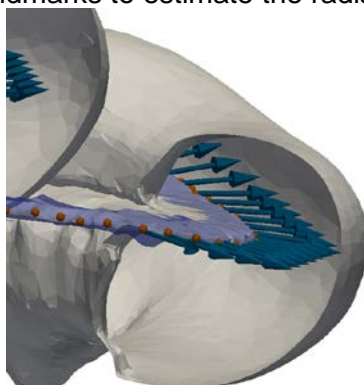

Figure 23: Estimation of basilar membrane position from landmarks on lamina spiralis ossea

Patient specific optimal map

Given the fact that the exact anatomical identity of the electrical excitation site on the nerve cell is not known and can be either the peripheral process ending in organ of Corti (OC) or the soma located in spiral ganglion (SG), the proposed patient specific optimal programming map is built as a trade-off between OC and SG stimulation. After the simulation of the implant position, it is possible to compute the frequencies corresponding to the maximum stimulation based on the minimum distance from each electrode to the organ of Corti and spiral ganglion, and the frequency mapping known from literature. Then, for each electrode an intermediate frequency is considered, with the constraint of being inside the frequency range of the sound processor and of not being too close to the neighboring frequencies.

Exploration of different model designs

The framework was first assessed on the models of electrode arrays used in clinical practice (Flex[28] and Standard) and the experimental design considering both stimulation scenarios (OC and SG). The performance of Flex[28]-based model was superior to the model of Standard electrode array, and the experimental design showed the best performance from all (Figure 24).
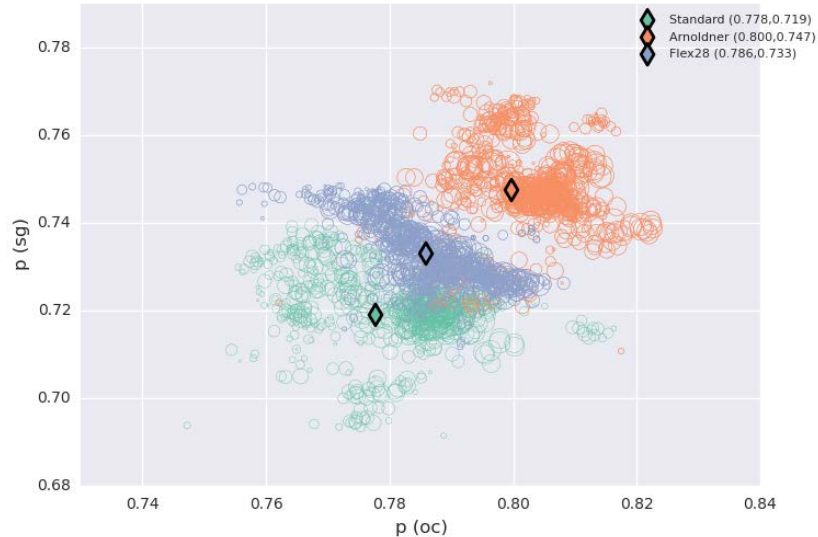
Figure 24: The performance score obtained by some known electrode designs on two stimulation cases: organ of Corti (oc) and spiral ganglion (sg) on samples uniformly sampled along the first 2 principal modes of variation. Each circle represents the score obtained on sample, and its size represents the likelihood of the shape. The diamond marker represents the weighted mean of the performances.

The final optimization was performed in the set of models which have a larger spacing between the electrodes at the apical end of the array, and adding more constraints derived from clinical and manufacturing considerations summoned in the Task T6.1 - "Parametric model of implant design". In particular, a) the number of electrodes has been kept to 12 in order to interface with the present speech processing strategies and b) the cross-section profiles along the length of the array and the length itself has been maintained the same as for the design of Flex[28] electrode array.
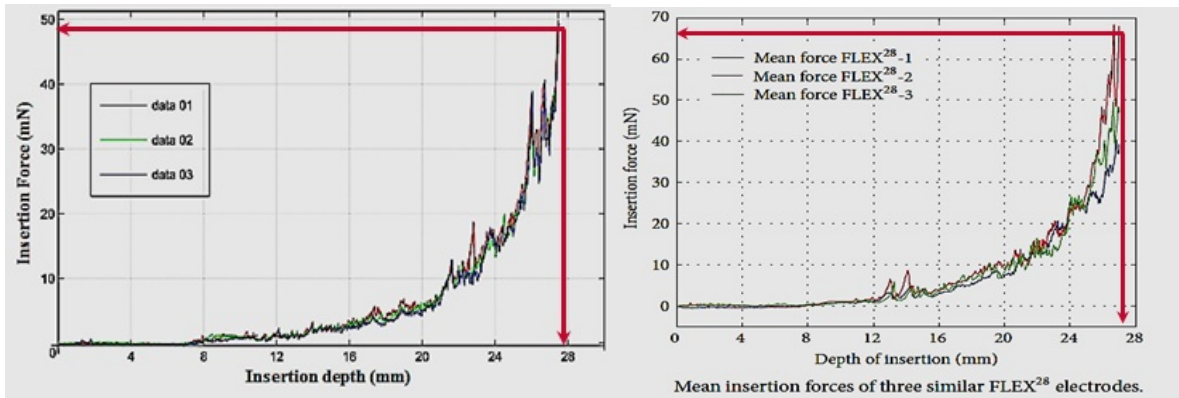
Novel electrode array design
The work carried out on this task was described in great detail in the delivery report D6.3 "Evaluation of new implant design" submitted in month 36.
The final design of the new electrode array was obtained after series of optimization steps considering both trauma to the cochlear structures during the insertion and functionality of the electrode array. A prototype of a new electrode array was then manufactured according to those specifications.

This new design was then validated in a series of experiments. First, the force measurements were carried out using a plastic model of human cochlea to determine the forces needed to insert such an electrode array as the changed positioning of electrode contacts, and particularly the presence of triple contacts in the apical end, could change the stiffness of the electrode array rod. Figure 25 shows that in fact the forces needed to achieve the full insertion, 28 mm, with the new design are even smaller than those needed for the original design (Flex[28]). Therefore, the insertion of this type of the electrode array should be as atraumatic as that of the Flex[28] design.

Figure 25: The measurement of insertion forces using the plastic model of the averaged sized human cochlea. Left: Forces associated with the insertion of the new electrode array design. Right: Forces associated with the insertion of Flex[28] electrode array. The x-axis refers to the insertion depth and y-axis shows the associated force needed to achieve such depth. Three independent measurements were carried out for each design and data ware highly reproducible.

Second, the Finite Element simulation techniques developed in WP4 and WP6 were used to compare *in-silico* the frequency-position mapping of electrodes in the new and original arrays and to estimate the coupling efficiency using the microCT images. The initiation of the excitation was expected to take place on the peripheral process of the nerves rather than on the soma, based on distance considerations in microCT images of implanted cochlea and previous experimental observations with patients implanted with Med-El cochlear implants. The Greenwood function was used to estimate the tonotopic map of the cochlea. The frequency mapping of the new optimized electrodes design according to their intracochlear position is shown in Figure 26 (left). For comparison, the simulation results with the Flex28 electrode array are also shown on the right. A comparison shows that the new design has a finer coverage of the speech region between 0.9 and 3 kHz due to the variable spacing as desired for better speech recognition.
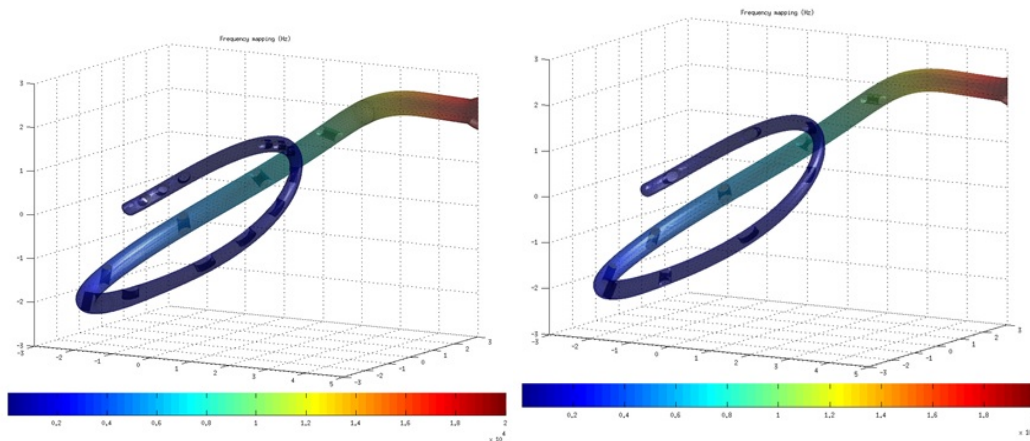
Figure 26: Computational simulation of the implanted cochlea with the optimized(left) and Flex[28](right) electrode array design. The color code of the frequency mapping according to the Greeenwood function

In-silico simulations of excitation spread plots for the standard Flex[28] design and the new design were also carried out and are shown in Figure 27. Each color represents a different electrode, starting from the most basal (C12) towards the most apical (C1). The curves show the potential field that reaches the organ of Corti due to the stimulation of a specific electrode. The horizontal axis shows the distance along the spiral ganglion and the vertical axis the measured stimulation. One can see that the two plots look very similar for the basal electrodes C7 to C12 (the first ones in the plot). They are evenly spaced and the only difference is due to the positioning of the CI electrode array during the simulated insertion.

The middle electrodes (C3 to C6) are much closer in the new design than in the standard one, and this is also reflected in the relevant plot. Eventually, the most apical electrodes (C1 and C2) stimulate in a similar way, even if in the new design their shape changed from one contact to three.
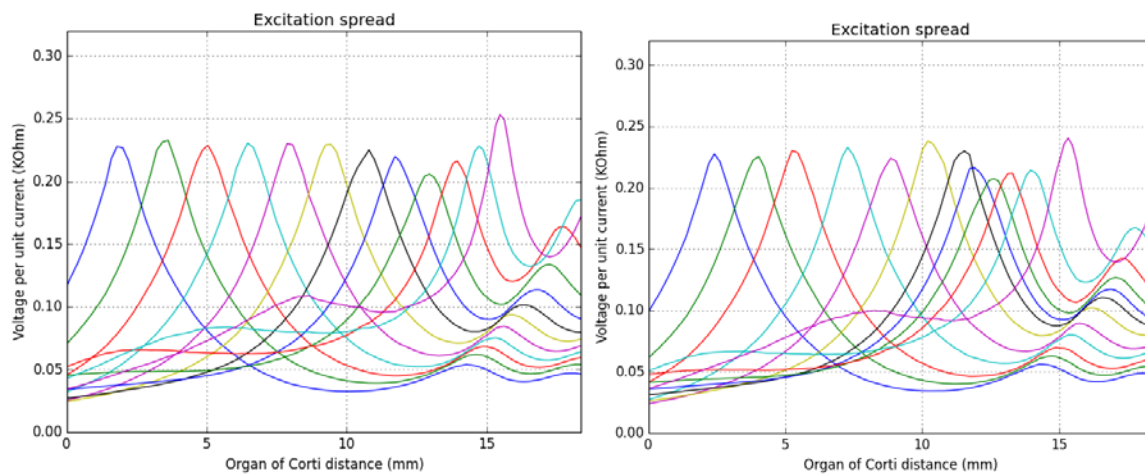
Figure 27: Excitation spread plots for (left) the standard Flex[28] and (right) the new electrode design. The horizontal axis show the distance along the spiral ganglion and the vertical axis the impedance measured. Each color corresponds to a different activated electrode.

Figure 28 compares such global effect for Flex[28] design on the left and the new design on the right.
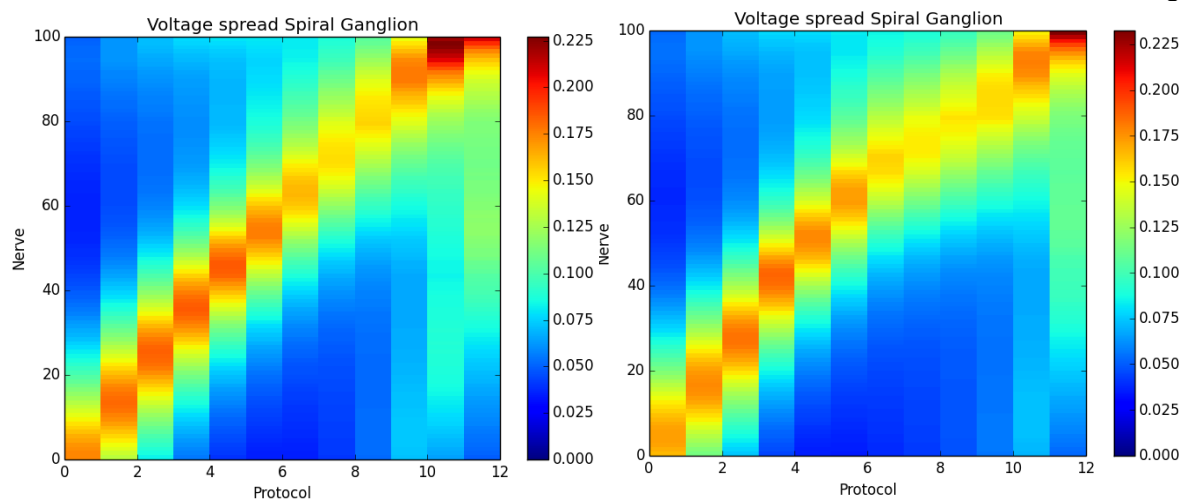

Figure 28: Comparison of the global electrical effect of the activation of all the contacts to the simulated cochlea for Flex[28] and new design (left and right, respectively). Each row represents the activation of one electrode (from the most basal one, C12 to the most apical one, C1) and each column represent one of the nerves that are tonotopically distributed along the spiral ganglion.

Novel accessory tools

A novel accessory tool was designed and developed to guide the insertion of an electrode array when the cochleostomy is used instead of the round window approach. The initial specifications for such a tool ware as follows: 1) inner diameter maximally 1.6 mm; 2) outer diameter for the insertion part between 1.8 mm and 1.6 mm; 3) handles at the non-inserted end of the tool to ease the device withdrawal after the completion of electrode insertion, large enough for comfortable fingers handling.

The prototype of such device according to desired specification was produced and is shown in Figure 29.
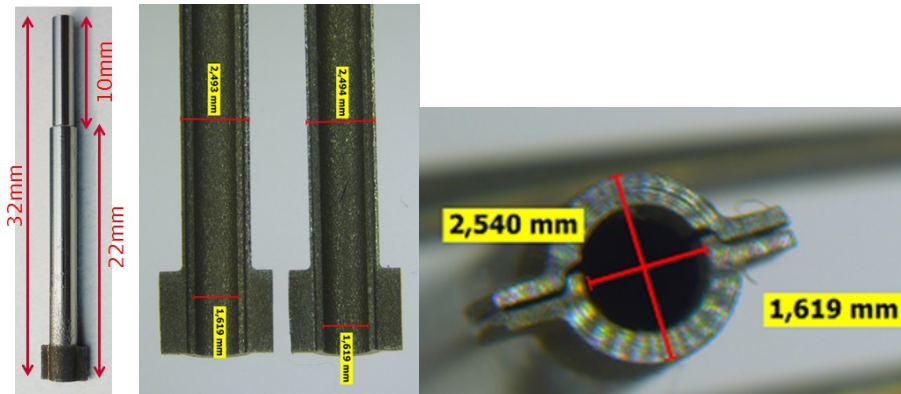
Figure 29: Prototype of the insertion tool. This tool is intended to facilitate the insertion of the electrode array in cases when requested by a surgeon due to particularly difficult accessibility. Left: assembled tool, Middle: two halves of the tool, Right: Detailed view of the assembled tool showing the "locking mechanism" keeping the two parts together.

Potential impact, main dissemination activities and exploitation of results (max 10 pages)

HEAR-EU has delivered a modular technology that will define and design a new generation of cochlear implants with optimal functional performance. This will significantly improve patient's quality of life until older age, thus increasing the number of healthy life years (HEALTH work program and EIP "active and healthy aging" impacts). Furthermore, it will also improve life expectations and performance for very young children allowing for even more efficient CI implantation at a very early age. Secondly, it will reduce the costs in European health care systems (HEALTH work program impact) by a reduction of hospitalization and surgery times regarding CI surgery. This will be achieved by making available computerized surgical planning and diagnostic tools. Importantly, improved functionality of CI (reduced stimulating electrical currents associated with hearing thresholds) will reduce battery consumption, again significantly lowering the running costs of this medical device. Moreover, HEAR-EU contributes to promoting the position of European industry in the EU and worldwide market of products and services associated to medical technologies (in alignment with the European Innovation Union Initiative and in particular with the EIP "active and healthy aging"). This is a global challenge that needs to be tackled from a global European perspective to combine capacities across different countries and build synergies in view of a world-wide market.

The synergy between medical (radiology, physiology) and computer sciences is a central aspect of this proposal. It leads to a new paradigm of interdisciplinary research towards the final aim of reducing in-vivo testing by enabling in-silico simulations (in alignment with the concepts of "in-silico medicine" and the "virtual physiological human"). Furthermore, the establishment of explanatory computer models for biological and clinical processes, such as those developed in WP3, contributes to the objectives of HEALTH-2012-2 by developing tools and methods for "increasing knowledge of biological processes and mechanisms involved in normal health and in specific disease situations, to transpose this knowledge into clinical applications including disease control and treatment".

In relation to specific impacts listed in HEALTH-2012-2.4.5-1, this project has developed: 1) highly automated imaging tools to facilitate individual-patient oriented cochlear implant surgery and 2) innovative design of cochlear implants (topic 2.4.5-1: "refined tools, technologies and procedures aimed at helping patients with sensory impairments to improve their quality of life"). Such tools significantly enhance adequate positioning and functional fitting of cochlear implant (bionic ear) for patients with profound hearing loss. Significant improvement in cochlear implant output is expected (20% reduction in thresholds), even under more difficult hearing conditions (topic 2.4.5-1: "implantable devices and artificial organs or their parts", and topic 2.4.5: "chronic diseases and improvement of quality of life"). Full attention is paid to "safety, bio-compatibility, interoperability and regulatory aspects" (topic 2.4.5-1), based on the expensive experience of the consortium, and in particular the industrial partners.

Further, this project also addresses the specific aspects of this call in order to encourage stronger SME efforts towards research and innovation (topic 2.4.5-1), through the involvement of two innovative SMEs, in collaboration with a large European enterprise.

The management provided the overall strategy and coordination to the project, the steering efforts of the partners for the achievement of milestones and ensuring that the work is undertaken with appropriate quality levels. Also we aim to set-up a project management structure that ensures an efficient operational management including administrative, financial and legal issues, supporting the Scientific Coordination in organising and supervising the pilot work and in its liaison with the European Commission. Finally, we will strive here to

support the appropriate communication and work dynamics to help drive the whole Consortium as a team towards successful completion.

All the dissemination and exploitation efforts of the projects were concentrated in WP8. We design a plan that allows for optimal communication within the project and the dissemination of information and knowledge generated by the project to relevant stakeholders. Also we disseminate the project knowledge and results to the research, clinical communities, as well as to the industry, the general public and patients. Finally, we develop an exploitation plan aiming at ensuring the use of the project results after the EC funding period.

Dissemination activities have been carried out at all levels, from specialist scientific conferences and industrial fairs to general dissemination events and appearances in newspapers and TV. A complete exploitation plan has been submitted in D8.6.

A brief summary of the results grouped by work package is below:

T8.1 - **Dissemination activities -** Following the communication plan(D8.1) dissemination has followed specific strategies targeting the different audiences. Dissemination to the general public was achieved with a website (D8.2, http://www.hear-eu.eu), a leaflet and appearance in several general media. Dissemination to the scientific community includes newsletters, institutional webpages, oral and poster presentations at scientific meetings and workshops. Several scientific papers have been published and also presented at international conferences. D8.3 reports the dissemination activities carried out by month 18, and D8.5 reports the dissemination activities carried out by month 36.

The strategy for communication and dissemination of the project was described in the Communication Plan (deliverable D8.1). A project website (documented in deliverable D8.2) has been created and maintained up to date. In a second iteration, the initial design of the website was modified in order to allow for more flexibility and improved aesthetic appearance. At month 18 of the project, an interim report on dissemination activities (deliverable D8.3) was submitted, giving an overview on the dissemination activities at that time. This final report is an updated version of the interim report, in which the activities of the second half of the project have been added.

Activities aiming at broad dissemination included the creation of a project leaflet, articles in newspapers and appearances in TV. Scientific articles in international conferences and journals have been produced, reporting the results of the project. Invited talks and contacts with researchers and clinical experts worldwide have been carried out.

During this project, HEAR-EU has organized three international workshops, and contributed to three more. We have actively reached out to other European research projects, and have established concrete collaborations with 5 consortia.

Companies participating in HEAR-EU have promoted awareness of the project in four industrial fairs. Policy makers and funding bodies have also been targeted, and three specific events are listed in this report, one involving the European Commission, another involving national administration in Spain, and finally an event at the United Nations headquarters in New York.

HEAR-EU has been featured twice as Success Story at the Horizon 2020 website.

T8.2 - **Exploitation scenarios -** The final exploitation plan (D8.6) has been submitted, indicating specific products and strategies of the partners.

Although exploitation activities are carried out and promoted by all partners of the consortium, the companies participating in the project have a leading role, for obvious reasons. In this deliverable, each of the three companies involved in the project report their intermediate exploitation plans. ALMA focuses on the development of novel surgical planning software, SCANCO reports their plans for the new high-energy micro-CT system, and MEDEL provide a business plan for the novel electrode designs that will be developed within HEAR-EU.

THE EXPLOITATION PLAN IS CONFIDENTIAL, as indicated by the classification as "Restricted" in the table of deliverables. Each company has prepared their section individually, and it has not been shared with other partners of the consortium. The project coordinator centralised the collection of the different documents and bundled them in a single document (D8.6) which is available for consultation to the EU officers.