

École polytechnique de Louvain

Predicting the outcome of cochlear implantation in adults with postlingual deafness via tractography of auditory and language pathway

Author: **Justine GOOSSE**

Supervisors: **Benoît MACQ, Laurence DRICOT**

Readers: **Nicolas DELINTE, Frédéric CREVECOEUR**

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Abstract

In recent years, cochlear implantation has revolutionized post-lingual deafness treatment, but predicting their outcomes still remains challenging. While many studies have focused on prelingual deaf children, this study aims to provide new perspectives in the field of cochlear implantation in postlingual deaf adults by correlating multiple diffusion measurements with different objective auditory tests, such as AWRS and DEWA. This study involves a cohort of 53 adult patients with postlingual deafness who underwent preoperative diffusion MRI scans. The DTI metrics of fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD), and streamline count of eight brain areas related to audition and language - the left arcuate fasciculus, the genu, body, and splenium of the corpus callosum, the right and left uncinate fasciculus, and the right and left inferior fronto-occipital fasciculus - were measured. The goal of this thesis was to use tractography to investigate white matter pathways related to audition and language in order to identify pre-operative DTI metrics that would influence post-cochlear implant outcomes. Two strategies were used to achieve it. For the first one, patients with an average postoperative word recognition score (AWRS) of 0.5 or more were classified in the "good outcome" group and those with a score of 0 in the "bad outcome" group. A two-sample t-test evaluation was performed to determine the significant variables between these two groups. The second consisted of a correlation analysis between post-cochlear implantation audiometric test results and pre-operative DTI measurements. The post-operative audiometric tests performed were the AWRS, the DEWA - an audio-visual integration test - and the categories of auditory performance (CAP). Results from the two strategies performed show a significantly better recovery audition (better AWRS and DEWA results) in patients with a better conservation of white matter integrity (lower MD and RD values, as well as higher FA values and streamline count) in the brain areas related to audition and language (left arcuate and uncinate fasciculus, corpus callosum, and left and right IFOF) before the cochlear implantation. Maintaining the microstructural integrity of these specific brain areas would therefore play a crucial role in the success of cochlear implantation in adults with postlingual deafness, offering new prospects for improving personalized hearing care.

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Acronyms

A1 primary auditory cortex.

A2 secondary auditory cortex.

AC Air Conduction.

AD Axial Diffusivity.

AF Arcuate Fasciculus.

AWRS Average Word Recognition Score.

CAP Categories of Auditory Performance.

CC Corpus Callosum.

CI Cochlear Implant.

CSF cerebrospinal fluid.

dB decibel.

DEWA Deggouj-Wathour.

DTI Diffusion Tensor Imaging.

EPI Echo Planar.

FA Fractional Anisotropy.

FID Free Induction Decay.

FOD Fiber Orientation Distribution.

HA Hearing Aids.

HL Hearing Loss.

Hz Hertz.

IFOF Inferio fronto-occipital fasciculus.

MD Mean Diffusivity.

MRI Magnetic Resonance Imaging.

RD Radial Diffusivity.

RF Radio Frequency.

RGB Red-Green-Blue.

ROI Region Of Interest.

SIR Speech Intelligibility Rating.

SPL Sound Pressure Level.

TE Time of Echo.

TR Repetition Time.

UF Uncinate Fasciculus.

WM White Matter.

WRS Word Recognition Score.

Introduction

Deafness is a profound sensory impairment that affects millions of people worldwide. In recent years, cochlear implantation has revolutionized the treatment of post-lingual deafness in adults, allowing individuals with severe hearing loss to perceive sound, giving them the opportunity to regain their hearing ability, and significantly improve their quality of life. Nevertheless, the cochlear implant is not a miracle solution. This success may vary among individuals, and some recipients may not achieve the same level of speech perception as others. Moreover, patients have to follow an intensive reeducation to be used to those new apparel and learn to recognize and interpret those new sounds. All this process takes time and requires energy and investment from the patient.

Advances in medical imaging techniques, such as DTI and tractography, have allowed scientists to investigate and visualize the brain in new ways. These techniques can highlight neuronal white matter pathways, such as those related to language and audition. Moreover, they provide metrics characterizing microstructural integrity through quantification of the diffusivity of water molecules in different directions. A great deal of research has been carried out to explore the white matter in deaf patients and controls, and to try to understand its reorganization. In addition, scientists are also studying the effects and results of cochlear implants in deaf people, and are attempting to unravel the mystery of performance variation by adults with cochlear implants. The ultimate goal is, therefore, to be able to predict, based on pre-op MRIs, whether or not it is worthwhile to cochlear implant a patient with postlingual deafness. This will avoid, in case of foreseeable failure, many costly and exhausting steps for the patient.

This thesis consequently focuses on identifying the preoperative parameters, i.e. the white matter regions and associated DTI metrics, that would influence the post-cochlear implantation outcomes via tractography. It focuses on postlingually deaf adults, a subject that has not often been addressed despite the fact that postlingual deaf people represent the majority of the deaf population. This study aims to fill this gap by exploring an area that has been little explored until now and by providing new insights.

This report consists of two main parts. The first part covers the theoretical concepts related to MRI and cochlear implants essential to the understanding of this thesis and includes two sections. The first one is dedicated to the concept of magnetic resonance imaging (MRI), focusing on the main principles of this technique, as well as on diffusion-weighted imaging and tractography. The second one is dedicated to audition and cochlear implants. It focuses on the audition in general, from the ear to the auditory cortex, before defining the concepts of deafness and cochlear implants. It concludes by describing the audiometric tests performed to measure a patient's hearing ability.

The second part focuses on the realization and analysis of tractography of auditory and language pathways. It contains three main sections. The first one describes the data and explains the methods used to perform tractography, as well as the strategies used to predict significant variables of cochlear implant outcomes. The second section gathers the results obtained after applying the different strategies and statistical analysis. Finally, the last section discusses the results obtained and compared the outcomes with those of previous studies. Lastly, the limitations of this study and possible improvements are exposed before summarizing the important findings of this research.

Part I

Theoretical background

Chapter 1

Magnetic Resonance Imaging

Magnetic Resonance Imaging (MRI) is a non-invasive imaging technology able to produce 2D or 3D images of the inside of the body.

In this section, key concepts of MRI will be developed. Diffusion-weighted imaging and tractography will also be covered.

1.1 Nuclear magnetic resonance

Nuclear magnetic resonance is the combination of three key elements: an atomic nucleus, a magnetic field, and a resonance phenomenon. The following subsections will explain those elements subsequently.

1.1.1 Magnetic resonance phenomenon

MRI, as every imaging technique, needs a starting point. For the MRI, this starting point is the hydrogen atom's nucleus. The reason for this choice is the abundance of H^+ in our body. It is indeed composed of approximately 2/3 of water, H_2O , and every molecule of water contains two hydrogen protons H^+ .

This proton possesses a positive charge and, when rotated, produces a spin around its axis. This spin is represented by the vector $\vec{S}$ and is an intrinsic property of the proton. A charged particle that rotates induces a magnetic field around itself, called a magnetic moment, $\vec{\mu}$ [1].

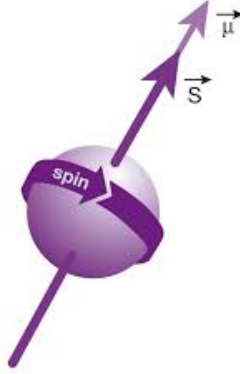


Figure 1.1: Spin $\vec{S}$ and magnetic moment $\vec{\mu}$ of a proton. From [1].

Those protons can be assimilated into small magnets. When they are no external magnetic field, those particles are randomly orientated. However, when protons are placed into a magnetic field $\vec{B}_0$, two phenomena appear.

First, the magnetic moment $\vec{\mu}$ of the proton will start rotating around the axes of $\vec{B}_0$ with a given angle at the Larmor frequency, creating a precession movement. The Larmor frequency is defined as :

$$\omega_0 = \gamma B_0. \quad (1.1)$$

Where ω_0 is the Larmor frequency also called precession frequency, and γ is the gyromagnetic ratio.

Secondly, as they act as small magnets, protons will align themselves with the magnetic field $\vec{B}_0$, either in the same sense as $\vec{B}_0$, parallel position, either in the opposite sense of $\vec{B}_0$, anti-parallel position. All the protons are divided into two groups: the parallel or spin-up and anti-parallel positions or spin-down.

When comparing those two groups, one can notice that the number of protons in the parallel position and in the anti-parallel position is not exactly the same: for two million protons, we will find around four protons that will be in excess in the parallel position. Even if this excess of protons in the spin-up position may seem negligible, it will cause the appearance of a macroscopic magnetization vector $\vec{M}$ [1, 2].

From a quantum point of view, those two groups correspond to two different energy levels. The anti-parallel position corresponds to the high-energy level and the parallel position to the low-energy level.

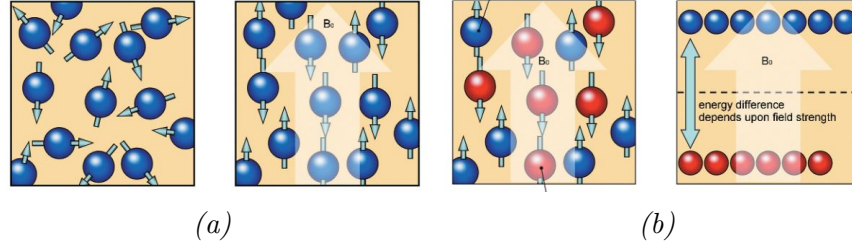


Figure 1.2: **(a)**: Alignment of the protons without (left) and with (right) the presence of a magnetic field $\vec{B}_0$; **(b)**: Quantum alignment of the protons, red particles corresponding to spin down, high energy level, and blue particles to spin up, low energy level. Adapted from [3].

When a body is placed into the magnetic field $\vec{B}_0$, the tissue will be magnetized. At equilibrium, this macroscopic magnetization vector $\vec{M}$ will be aligned with $\vec{B}_0$ on O_z , without any components in the transversal plan xOy because they are out of phase. Therefore, the only remaining component will be the longitudinal one. However, compared to a magnetic field $\vec{B}_0$ of 1.5 or 3 Tesla, this resultant component $\vec{M}$ is infinitely too small to be detected. To measure it, we need to tip the spins by 90° in the xOy plan [1, 4]. Here we introduce our third key concept: the resonance.

The resonance is the transfer of energy between two systems at the same frequency. In MRI, this resonance is obtained with a magnetic wave of radiofrequency, the RF wave. This RF wave has the same frequency as the Larmor frequency. The consequences of the 90° RF waves on $\vec{M}$ can be decomposed in two moves (see Fig. 1.3). Firstly, this RF wave at the resonance frequency gives the amount of energy equal to ΔE , the difference between the low-level and high-level energy. It results in the transfer of protons from the low-energy level to the high-energy level. Therefore, there is an equalization of the number of protons from the two groups on the two energy levels, leading to a zero longitudinal component. The second "move" consists of re-phasing protons. It involves the growth of $\vec{M}_{xy}$, which becomes maximal [1, 2, 4, 5]. As those two moves are produced simultaneously, it results in a tilt on 90° of $\vec{M}$.

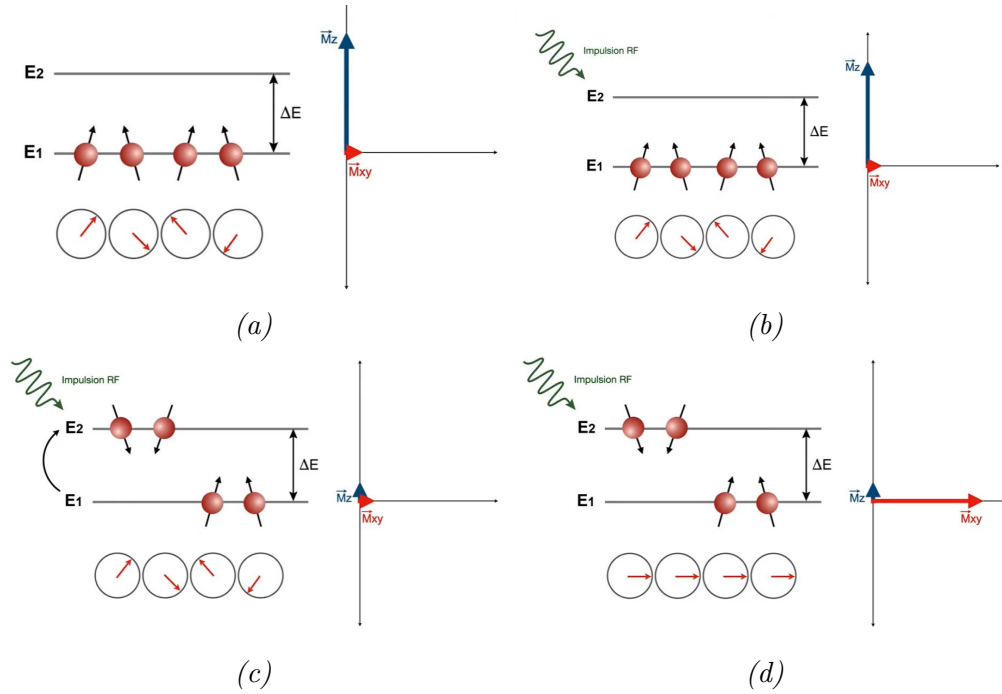


Figure 1.3: Decomposition of the phenomenon of reasoning. It starts with the equilibrium (a), the RF impulsion (b), followed by the transfer of energy (c) leading to a zero longitudinal component. Then, we can see the re-phasing of the proton (d), involving the growth of $\vec{M}_{xy}$. Adapted from [4].

It is also possible to produce a 180° tilt by doubling the time of the RF wave or its intensity. It will lead to an inversion of the vector $\vec{M}$ [1].

1.1.2 Relaxation

When the RF impulsion stops being emitted, we will observe the two inverse moves. First, protons transferred to the high-energy level will come back to the low-energy level, resulting in the regrowth of M_z . Second, protons that were in phase during the excitation phase will go out of phase, causing the transverse component to disappear. This phenomenon is called relaxation. We will distinguish three different relaxations: the T_1 relaxation or relaxation "spin-network", the T_2 relaxation or relaxation "spin-spin", and the T_2^* relaxation [1, 2].

T1

The 90° RF wave leads to the disappearance of the longitudinal component M_z and the growth of the transversal component M_{xy} . This change is caused by protons moving from the low-energy level to the high-energy level. As this system is unstable it will return to equilibrium when the RF wave will stop to be emitted. Protons will come back to the low-energy level, and the longitudinal component M_z will regrowth. This is the T_1 relaxation. It is characterized by a time T_1 , representing the time required for the tissue to regrow the longitudinal magnetization. As it can be seen in Fig.1.4, the longitudinal relaxation T_1 is represented by an increasing exponential. T_1 varies from one tissue to another and depends on the mobility of molecules involving protons. In biological media, molecules undergo permanent translation, rotation, and collision (Brownian motions and collisions), which can be characterized by the frequency of molecular collisions. Spin-lattice relaxation (energy absorption grid) is more effective for collision frequencies closer to the Larmor resonance frequency. Therefore T_1 will be longer in liquids than in solids and shorter in fatty tissue [1].

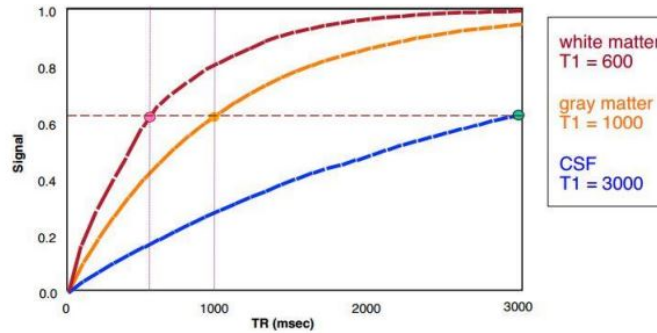


Figure 1.4: T_1 represented for three different tissues: the grey matter, the white matter, and the cerebral spinal fluid. Adapted from [2].

T2

When the system returns to equilibrium, protons will go out of phase, and the M_{xy} which had reached a maximal value due to the re-phase of the protons will return to zero. This step is called the T_2 relaxation or transversal relaxation and can be represented by a decreasing exponential, as illustrated in Fig. 1.5. As for T_1 , T_2 will vary with tissues. T_2 is influenced by the heterogeneity of the molecular environment. Protons experience distinct molecular conditions where minor magnetic fields add up to the main magnetic field. As a result, spins naturally rotate

at slightly different angular velocities compared to ω_0 , causing them to desynchronize. In liquid environments, the Brownian motion of small molecules causes these minor fields to cancel out (averaging), resulting in fewer small local magnetic fields contributing to T_2 relaxation (proton dephasing). Consequently, T_2 is prolonged. Conversely, in solids or large molecules, the local molecular fields persist, leading to a shortened T_2 [1].

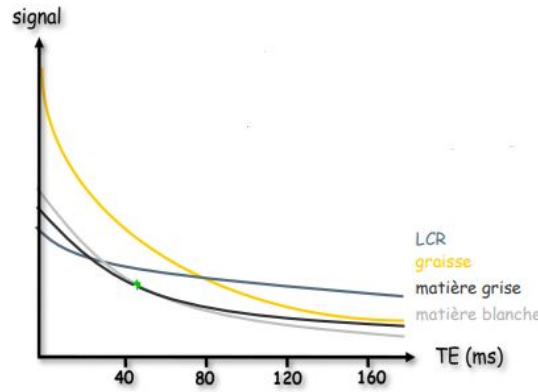


Figure 1.5: T_2 represented for four different tissues: spinal fluid (dark grey), fat (yellow), grey matter (dark), and white matter (light grey). Adapted from [2].

T_2^*

With a coil equivalent (antenna) the transverse magnetic vector can be recorded in motion. It is a sinusoid of constant frequency damped by an exponential of time. This damped sinusoid is called a Free Induction Decay (FID). The envelope of the FID is a decreasing exponential in T_2^* and not in T_2 because this curve is influenced by two types of field heterogeneity of the magnetic field. First, a field heterogeneity of molecular origin which in isolation is responsible for the so-called T_2 transverse decay. And secondly, heterogeneity of the field B_0 on a microscopic scale (constant over time) accelerates the transverse decay, known as T_2^* . T_2^* is therefore always shorter than T_2 . After a 90° RF pulse, the signal decays faster than it should [1, 5].

1.1.3 Spin Echo sequence

A spin echo sequence is an MRI sequence consisting of a succession of 90° impulse followed by 180° impulse. The 180° rephasing pulse compensates for constant field heterogeneities and provides a T_2 -weighted echo instead of T_2^* .

After the 90° pulse, the protons lose their phase coherence during the spin-spin relaxation. This phase shift results in a decrease in transverse magnetization.

If a 180° pulse is applied after a 90° pulse, the protons that were precessing last precess first and vice versa, which restores the phase coherence (rephasing). However, it can be seen that the transverse magnetization vector during the rephasing does not recover its maximum value. Indeed, the 180° impulse neutralizes the constant field heterogeneities (B_0 's own heterogeneities...) but does not neutralize heterogeneities of molecular origin. The attenuation of the signal, therefore, corresponds to the T_2 properties of the tissue [1, 5].

The repetition of the 90° and 180° impulse is consequently the base of the spin echo sequence. As you can see in Fig.1.6, this sequence relies also on two important parameters: the Time of Echo (TE) and the Repetition Time (TR). The repetition time, TR, is the amount of time between two successive 90° pulses, and the time of echo, TE, is the time between the 90° impulsions and the receipt of the echo signal. We can also notice that the 180° impulse is emitted at time $TE/2$.

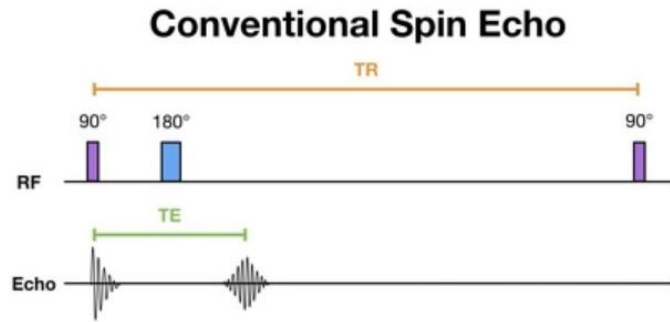


Figure 1.6: Spin echo sequence. The repetition of a 90° impulse (purple) followed by a 180° impulse (blue) is represented on the RF line. The TR separates two 90° impulsions and the TE separates the emission and the receipt of the echo signal. The latter is represented on the Echo line. From [6]

1.1.4 Image contrast

As seen previously, every single tissue possesses its own behavior depending on the weighting of the signal according to T_1 or T_2 . Those properties will help us to distinguish one tissue from another. In MRI, three different types of contrasts exist: T_1 contrast, T_2 contrast, and proton density contrast. They are weighted with the parameters TR and TE of the Spin Echo sequence. We will focus on the T_1 contrast.

The T_1 contrast is obtained with a short TE and a short TR. TR weights the T_1 sequence. If we compare two tissues with different T_1 , one short and one long, and if we take a long TR (i.e. wait a long time), we will observe that both tissues would have almost reached the equilibrium. The contrast in T_1 between them will therefore be weak. On the contrary, if we use a short TR, and so detect the signal after a shorter amount of time, the contrast between them will be higher due to their different regrowth speeds (see Fig. 1.7). The tissue with the shorter T_1 will give the highest signal and will be the most white on images. A short TE will so weight the T_1 sequence while a long one will unweight the T_1 sequence. To minimize the T_2 effect, a short TE will be combined with a short TR [1].

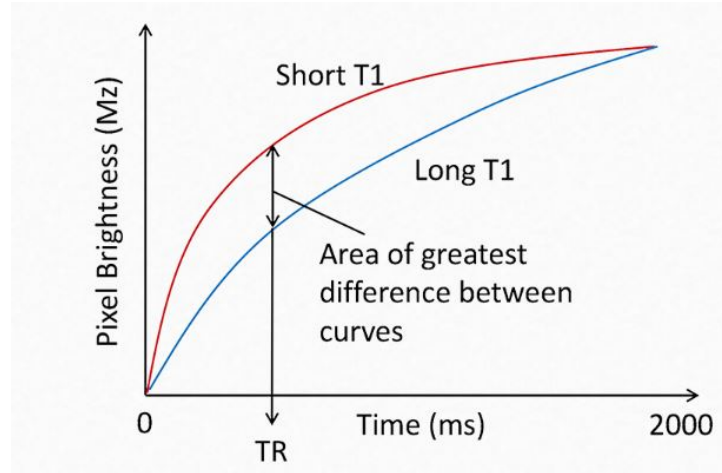


Figure 1.7: T_1 contrast. The abscissa axis represents the regrowth time (ms), and the ordinate axis the pixel brightness (Mz). The higher the pixel brightness, the whiter the tissue will appear. We can see that with a short TR, there is a greater difference between the T_1 curves. The tissue with the shortest T_1 (red) will be the whitest. Conversely, if we wait longer (longer TR), the two curves will have almost reached equilibrium. The difference in brightness between the two will be almost zero, leading to poor contrast between the two tissues. From [7].

1.2 Diffusion Weighted Imaging

Diffusion imaging is a form of MRI based on the microscopic movements of water molecules in the tissues. In a liquid, water molecules are not still, they are subject to random and permanent movement: Brownian motion [1]. In tissues, diffusion will be more or less high depending on the obstacles encountered. The more obstacles the water molecules encounter (more structured tissues), the weaker and slower their progression will be because movement will be more difficult.

It is for example the case in white and grey matter. Conversely, if they encounter fewer obstacles (less structured tissue), the movement of water molecules will be faster and higher, because the water can circulate more freely, as in the cerebrospinal fluid (CSF).

In practice, diffusion imaging will be performed with an Echo Planar (EPI) sequence and the addition of diffusion gradients, applied on both sides of the 180° impulse, as illustrated in Fig. 1.8.

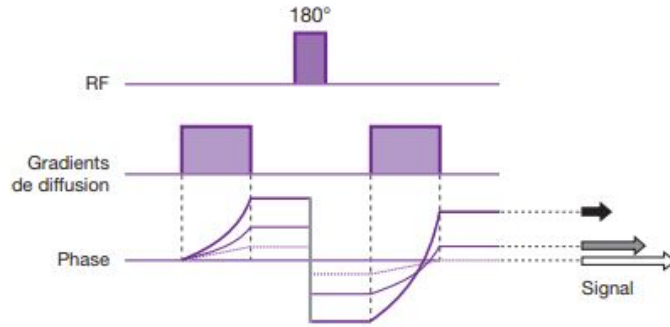


Figure 1.8: Gradient diffusion principles. Diffusion gradients are applied on both sides of the 180° RF impulse. For stationary protons, the dephasing caused by the first gradient will be compensated by the second one, and the signal will not be lost. On the contrary, for moving protons, this dephasing will not be compensated and the output signal will be decreased. The greater the molecular movement (the darker the arrow), the greater the signal loss. From [1].

For stationary protons, the dephasing caused by the first gradient will be compensated by the second one, and the signal will not be lost. Nevertheless, if protons are in motion, as is the case for those on water molecules, the dephasing caused by the first gradient will not be compensated by the second one, due to the molecular movements, leading to a decreasing signal. This signal loss will be as high as the molecular motion is high. As it modifies the intensity of the output signal, diffusion gradient will play an important role in coding diffusion MRI. To resume, on one hand, regions with a low molecular diffusion, where protons are quite stationary will present a hyper-signal. On the other hand, regions with a high molecular diffusion, where protons are in motion, will give a weak output signal.

The output signal, therefore, depends on the diffusion coefficient of tissues, D . But it also depends on another parameter, b , which depends on the performance of the gradients used :

$$S = S_0 e^{-bD}, \quad (1.2)$$

where S represents the signal with diffusion gradient and S_0 without it.

This parameter b is calculated according to the amplitude of the diffusion gradients G , their time of application, τ , and T , the time between the application of the two gradients [1]:

$$b = (\gamma G \tau)^2 (T - \tau/3), \quad (1.3)$$

where γ is the gyromagnetic ratio.

Increasing b will therefore increase the sensitivity of the sequence to the phenomenon of molecular diffusion.

An MRI diffusion sequence is made of three successive EPI sequences. Diffusion gradients are applied in three different directions, in the axis of the slice selection, the axis of phase encoding, and the one of frequency encoding. It leads to three images generated per slice, diffusion-weighted in each direction. A fourth image is usually made by combining the three previous ones, called trace image [1, 4].

1.2.1 Diffusion Tensor Imaging

Diffusion Tensor Imaging (DTI) is a technique providing specific information about the structural integrity and directional orientation of the white matter tract, while MRI techniques rather consider the white matter as a homogeneous tissue [8].

In medical imaging, information is represented in voxels, the 3D equivalent to 2D pixels. In each voxel, we can describe the behavior of the water molecule diffusion. It could be either isotropic or anisotropic. Diffusion is said to be isotropic when the diffusion of water molecules is the same in every direction. This is the case, for example for the CSF.

In contrast, in more structured biological tissues, as in the white matter, molecule diffusion is said to be anisotropic. The diffusion of water molecules is facilitated along the axonal fibers but is reduced perpendicularly to the fibers. Fig.1.9 illustrates those differences.

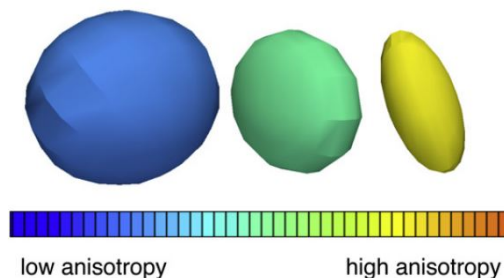


Figure 1.9: Differences in tensor anisotropy and orientation. From [9].

To describe more precisely the movement of anisotropic water molecules, we will describe here a new mathematical concept: the diffusion tensor.

This tensor is a three-dimensional structure. It is represented with a 3 by 3 symmetric matrix where the diagonal elements of this tensor represents diffusion along the three main axes :

$$D = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{pmatrix}.$$

From this diffusion tensor, four metrics can be obtained from λ_1 , λ_2 and λ_3 , the three eigenvalues of the diffusion tensor represented in Fig. 1.10 for an isotropic and anisotropic diffusion. Those four metrics can be used to assess different properties of the brain's fiber bundles and are listed below.

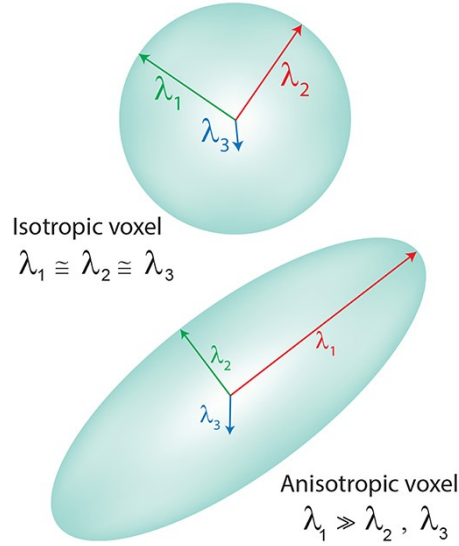


Figure 1.10: Eigenvalue of the diffusion vector. From [10].

Mean Diffusivity - MD

Mean Diffusivity (MD) corresponds to the average of the tensors eigenvalues and it is linked to the diffusion of water in the extracellular space [9]. MD is also often taken as an indicator of white matter damage. MD increases when myelinated is absent and conversely, it is lower in the presence of myelin [11].

$$MD = \frac{Tr(D)}{3} = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}. \quad (1.4)$$

Notice that MD values (as RD and AD values explained below) are between 0 and $3 \cdot 10^{-3} \text{ mm}^2/\text{s}$.

Fractional Anisotropy - FA

Fractional Anisotropy (FA) is the most used metric. This measure quantifies the fraction of diffusion that is anisotropic. It is also considered as a measure of white matter integrity, such as high values of FA representing high WM integrity [9]. We can also notice that the output is a value between 0 and 1.

$$FA = \sqrt{\frac{1}{2} \frac{(\lambda_1 - \lambda_2)^2 + (\lambda_2 - \lambda_3)^2 + (\lambda_3 - \lambda_1)^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}. \quad (1.5)$$

Axial Diffusivity - AD

The Axial Diffusivity (AD) represents the diffusivity along the principal axis of the diffusion and it is therefore only given by λ_1 . Low AD values may signify axonal injury, reduced axonal caliber, or less coherent orientation of axons [12].

$$AD = \lambda_1. \quad (1.6)$$

Radial Diffusivity - RD

Radial Diffusivity (RD) shows the water diffusivity perpendicular to the principal axis and high RD values may reflect myelin perturbations. Changes in the axonal diameters or density may also influence RD [13].

$$RD = \frac{\lambda_2 + \lambda_3}{2}. \quad (1.7)$$

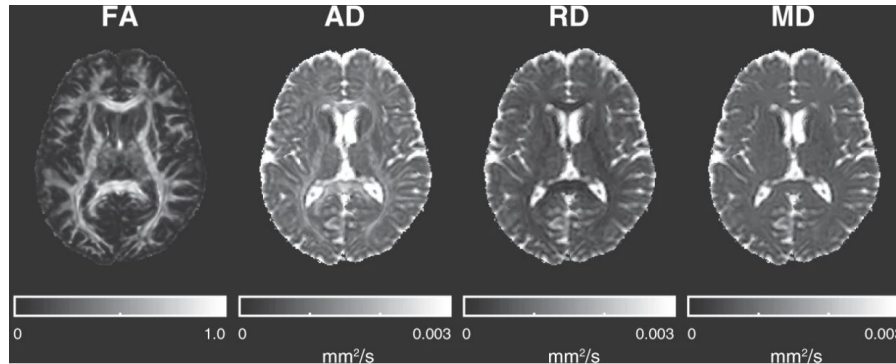


Figure 1.11: Illustration of the four metrics. From left to right: an axial slice of FA map, AD, RD, and MD map. Adapted from [14].

1.2.2 DTI limitations

Although DTI is a powerful tool for visualizing white matter, it has some limitations. One of the most significant limitations is the inability of the model to follow a non-Gaussian distribution. Therefore, only a population of a single

fiber can be modeled at each imaging voxel. This becomes problematic when there are multiple fiber populations passing through them or when the fiber bundles are highly curved. Another problem is the crossing fiber. When fibers cross each other within the same voxel, the main diffusion direction given by the diffusion tensor will not correspond to a real trajectory and can distort results [15].

1.3 Tractography

Tractography is an MRI technique using diffusion tensor data to highlight neuronal white matter pathways. As mentioned above, the diffusion tensor provides information about the direction of the water molecules inside each voxel, and by extension of the fibers. Therefore, knowing the orientation of fibers at every voxel allows us to reconstruct complete tracks by joining all of them [16].

In a simple way, it consists of "planting seeds" at some desired locations, and letting them extend by following the preferred direction until they reach a new voxel. The process will therefore connect voxels together, by continuously updating the preference direction, until a tract is formed [16]. An example of a tractogram is shown in Fig.1.13.

To generate those tracts, multiple tractography algorithms exist. Here, we will describe the two more known algorithm families: probabilistic and deterministic [17, 18]. The difference between those algorithms in tractography relies on their approach to estimating connections between brain regions from imaging data.

On one hand, the probabilistic algorithms are based on a model that includes uncertainty [16]. It means that the selection of the tracking direction at each point along the path is randomized, drawing from a distribution. This distribution varies at each point and is influenced by the observed diffusion data available at that specific point. They generally use methods based on diffusion theory, such as Fiber Orientation Distribution (FOD) [19]. They estimate the distribution of small fiber bundles between different brain regions using probabilistic information about water diffusion. These probabilistic approaches can provide more accurate and flexible results, especially when capturing complex connections or in areas where imaging data is less reliable. However, it is possible for probabilistic tractography algorithms to encounter limitations. In some cases, they may fail to identify existing pathways that are known to be present. Conversely, there are instances where these algorithms may generate paths that appear to exist, even though they are not anatomically accurate [16].

The deterministic algorithms, on the other hand, do not take into account any uncertainty along the path of the track [16]. They use specific rules to track fiber trajectories through the brain, such as following the primary diffusion direction [20]. They can provide fast and reproducible results, but may also be sensitive

to model errors and may not capture the complex connections in the brain. Differences between those two algorithms are schematically illustrated in Fig.1.12.

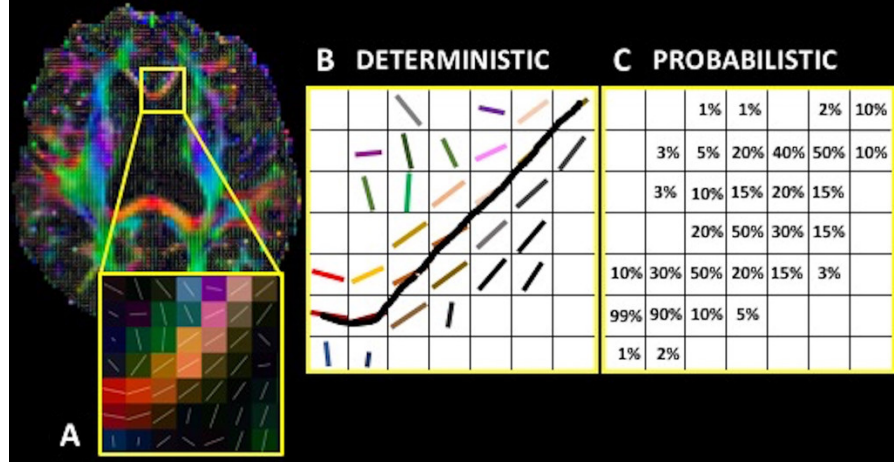


Figure 1.12: **A:** Degree of anisotropy. **B:** Deterministic fiber tracking involves inferring the fiber path through voxels based on a single diffusion orientation within each voxel. **C:** Probabilistic fiber tracking generates tractography by considering a probability distribution of diffusion orientations within each voxel. Adapted from [21].

Probabilistic tractography will be used in this thesis, as it has been demonstrated that probabilistic tractography could offer advantages over deterministic tractography. They can enhance sensitivity in accurately representing known tracts, as well as detect a greater number of fibers [21].

Tractography is usually illustrated in a 3D plan with standard Red-Green-Blue (RGB) color code allowing us to understand the orientation of fibers at every voxel and their anisotropy [22]. Fig. 1.13, representing the corpus callosum, a network of white matter that connects the two hemispheres of the brain, is a telling example to understand this color code:

- Red fibers: indicate directions on the X-axis (right to left or left to right).
- Green fibers: indicate directions along the Y-axis (posterior to anterior or anterior to posterior).
- Blue fibers: indicate directions along the Z-axis (top to bottom or bottom to top).

Tractographies presented in this thesis were visualized through the TrackVis program [23].

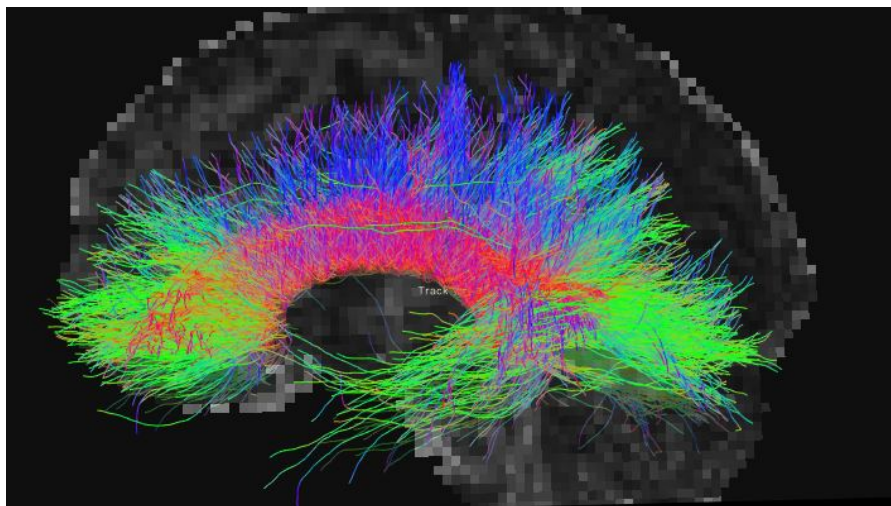


Figure 1.13: Tractogram example: probabilistic tractography of the corpus callosum.

Chapter 2

Deafness and Cochlear Implant

2.1 Audition

Every sound we hear is actually a sound wave. The whole hearing process is based on the propagation of these sound waves in the ears and their recognition by the brain [24].

2.1.1 Anatomy of the ear

The ear consists of three main parts. All of these play an essential role in the hearing process (Fig 2.1). Firstly, the outer ear consists of the auricle and the external auditory canal. The outer ear is used to pick up sounds and amplify them. It is also used to localize sounds. The sound waves then continue into the external ear canal. The second part of the ear, the middle ear, consists of the eardrum and the chain of ossicles. The sound waves reach the eardrum, which acts as a drumhead and collects the vibrations over a large area [25]. It then causes the ossicles to vibrate and these vibrations are transmitted to the inner ear. Since the inner ear is composed of fluid and the outer ear of air, the ossicles also act as an impedance adapter between the middle and inner ear. When the vibration finally reaches the inner ear, it enters an organ called the cochlea, a spiral-shaped structure. It is lined with hair cells, which are activated by a specific movement, depending on the sound frequency. When these cells are activated, the signals are sent to the auditory nerve and then to the brain, where they are interpreted as sound [26].

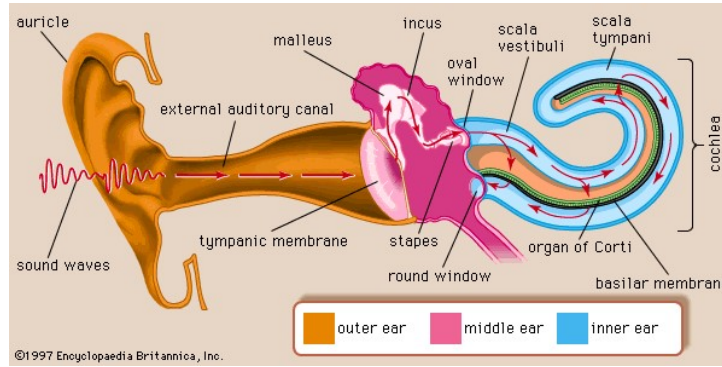


Figure 2.1: Human ear anatomy. The orange part represents the outer ear, with the auricle. The pink part illustrates the middle ear with the tympan and the ossicle chain and the blue part is the inner ear, with the cochlea [26].

2.1.2 Ascending auditory pathways

After being collected by the ear, sounds will be converted to the brain via a short and fast pathway leading to the primary auditory cortex: the ascending auditory pathways [25]. This pathway starts at the auditory nerve and transmits auditory information through a series of nuclei to the cortex where perception occurs [27]. The information, therefore, passes through the cochlear nucleus, the superior olivary nuclei, the lateral lemniscus, the inferior colliculus, and finally, the medial geniculate nuclei [28]. Each nucleus works on decoding and interpreting the information provided by the cochlea in a specific way and then transmits it to the next relay.

The ultimate point of this pathway is the auditory cortex. Its purpose is to identify, segregate and, localize sounds in space. A distinction can be made between the primary auditory cortex, A1, and a secondary auditory cortex (A2), or belt areas [29].

The primary auditory cortex (A1), represented in blue in Fig. 2.2, lies in the superior temporal gyrus and extends into the lateral sulcus and the transverse temporal gyri or Heschl gyrus. It receives direct input from the ventral division of the medial geniculate complex. As a result, A1 has a well-defined tonotopic map. As for the cochlea, the auditory cortex is organized in a way that different zones of the cortex correspond to specific sound frequencies, neighboring frequencies remaining close to each other [29]. The lower frequencies correspond to the frequencies located in the apex of the cochlea, while the higher frequencies correspond to those located in the base of the cochlea. This tonotopy starts from the cochlea and remains during all the auditory pathways, until the auditory cortex.

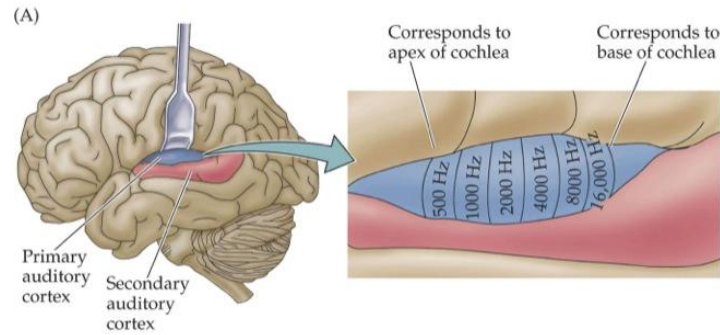


Figure 2.2: Human auditory cortex. The blue part corresponds to the primary auditory cortex. It conserves the tonotopy of the cochlea. It is surrounded by the secondary auditory cortex represented in pink. From [29].

The belt areas or secondary auditory cortex, represented in pink in Fig. 2.2, surrounds the primary auditory cortex and receives afferents from the dorsal and medial subnuclei of the medial geniculate nucleus [30]. It receives less focused input from the belt areas of the medial geniculate complex and is, therefore, less organized in its tonotopic arrangement [29]. This zone plays an important role in sound localization as well as in analyzing complex sounds, such as human language [31]. In the posterior part of the secondary cortex (in the left hemisphere only), we found Wernicke's area (see Fig. 2.3) [32]. This region is dedicated to the comprehension of the language.

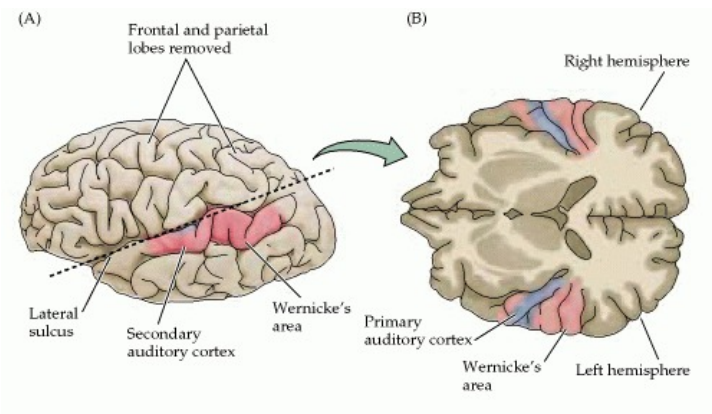


Figure 2.3: Human auditory cortical areas related to processing speech sounds. The primary auditory cortex is presented in blue and the secondary auditory cortex in pink. The Wernicke's area is located in the posterior part of the secondary cortex, in the left hemisphere. From [29].

2.1.3 White-matter pathways involved in auditory processing and language

Our central nervous system is composed in a very synthetic way of two parts: the grey and the white matter. The grey matter is mostly made up of neuronal cell bodies and this is the location where the main processing is done [33]. The white matter corresponds to the communication channels and is constituted of a high concentration of myelinated axons.

In this thesis, we seek to understand the possible pathways between regions of the brain related to the hearing and language process, and how the information is traveling between those parts. Therefore, we will focus on analyzing the white matter.

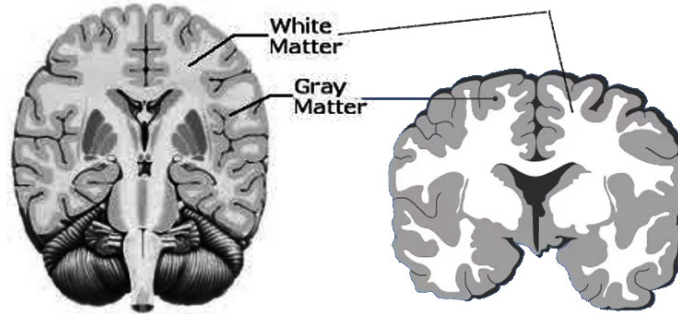


Figure 2.4: Human grey and white matter. From [34].

To predict cochlear implant outcome of postlingually deaf patients, we will focus on some regions of interest in white matter :

- Central auditory pathways
- White matter near auditory cortex (superior temporal gyrus including Heschl's gyrus)
- White matter bundles related to hearing and language [35]: arcuate, uncinate, and inferior fronto-occipital fasciculus, represented in Fig. 2.5

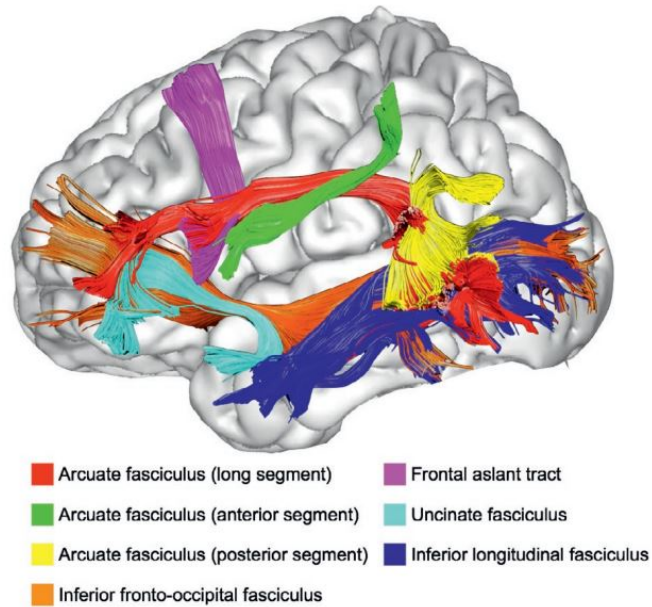


Figure 2.5: Tractography reconstruction of the major association pathways involved in auditory processing and language. From [35].

When speaking about language, we need to link two specific zones of the brain: Wernicke's area and Broca's area. The first can be interpreted as the zone of the comprehension of the language, and the second one as the production of the language [25]. The Broca's area is located in the left frontal lobe of the brain and is also dedicated to the control of movement related to speech [36]. Those two zones are connected together by a network of neural white matter fibers: the arcuate fasciculus (Fig. 2.6)[37].

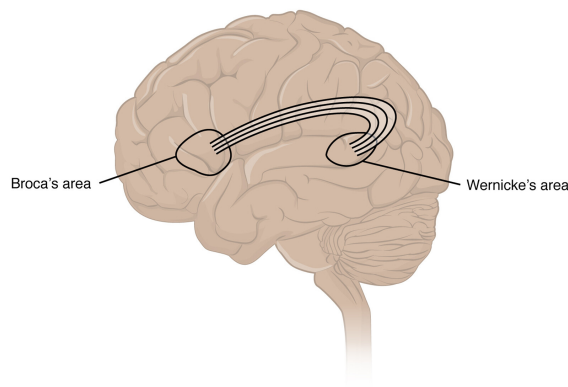


Figure 2.6: Arcuate fasciculus connecting the Brocas' area with the Wernicke's area. From [38].

In addition to the Arcuate Fasciculus (AF), the Uncinate Fasciculus (UF) is another language-related white matter pathway exhibiting structural asymmetries. The uncinate fasciculus is a long-range association pathway connecting the anterior temporal lobes bi-directionally to the anterior prefrontal and lateral orbitofrontal cortex (represented in light blue in Fig. 2.5). The precise functional role of the uncinate fasciculus is not yet fully understood, but empirical evidence suggests a role for language as well as episodic memory and social-emotional processing [39]. It could also play an essential role in lexical retrieval, semantic associations, and naming [35]. It was also suggested that the uncinate fasciculus may play a role in sound recognition because of the areas it connects [40].

The Inferio fronto-occipital fasciculus (IFOF), represented in orange in Fig. 2.5, is a sizable and intricate white matter pathway extending from the parietal and occipital lobes to the frontal lobe, taking a convoluted course alongside the insula [41]. As for the uncinate fasciculus, the role and function of the IFOF are not completely understood. Nevertheless, previous studies suggest that it could play a vital role in processing semantic language, directing goal-oriented actions, and facilitating visual task switching [41].

There are also some regions of white matter, shown in Fig. 2.7, that were identified as different between postlingually and control patients in the literature [42, 43, 44, 45]:

- Corpus callosum (genu, body, splenium)
- Fornix
- Inner and outer capsules
- Fasciculus connecting the hippocampus and the lingual gyrus (at the medial side of the occipital lobe), and the hippocampus and the cingulate gyrus (cingulum)

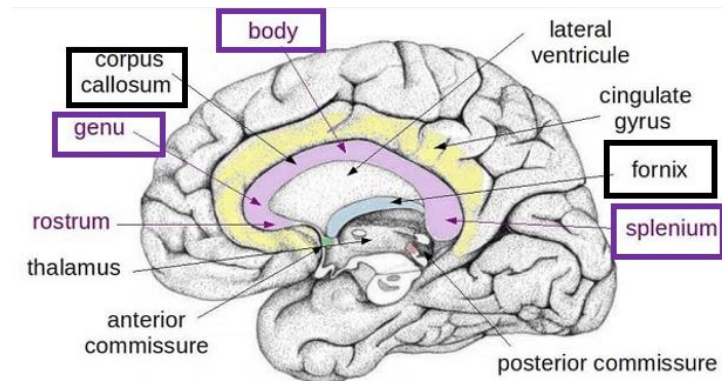


Figure 2.7: In frame, regions of white matter identified as different between postlingually and control patients. From [46].

The Corpus Callosum (CC) is a structure of the brain establishing a connection between the left and right cerebral cortices. Nowadays, it is widely recognized as one of the most extensively researched and comprehensively understood white matter structures [47]. Due to its size, the corpus callosum has been divided into several parts in order to be studied more precisely. In papers studying white matter changes in people with hearing loss, the CC has been studied into three parts: the genu, the body, and the splenium. The genu is the rostral part of the corpus callosum. It links together prefrontal association areas and anterior inferior parietal regions. The splenium, the caudal end of the corpus callosum, connects parietal and temporal lobes association areas as well as occipital lobes. And the body, which is the central portion of the CC, joints premotor and supplementary motor areas and also connects primary motor areas [43, 45, 47, 48]. Those three parts are illustrated in Fig. 2.7. Nevertheless, other DTI studies divided the corpus callosum into more than three parts. L. Concha et al. used a separation into five parts for their study of epileptic patients [49], when Y. Ohoshi et al. proposed a tractography of the corpus callosum into seven separate segments in their analysis study of schizophrenia [50], and C. Xue et al. segmented it into six parts when studying adolescents with idiopathic scoliosis [51]. Although various segmentations are possible, the most common is the division into five parts (genu, the rostrum, the body, the isthmus, and the splenium) [52].

2.2 Deafness

As every part of the human body, the ear may not work correctly. Depending on the area of the ear affected, the hearing loss will be more or less severe and how it is treated will change drastically.

There exist four different types of hearing loss [53] :

- Conductive hearing loss: it is caused by something preventing sound from passing through the outer or middle ear. It can often be treated with medication or surgery.
- Sensorineural hearing loss: it is provoked by a problem in the inner ear (as missing or damaged hair cells in the cochlea) or in the auditory nerve.
- Mixed hearing loss: it is a hearing loss combining both conductive and sensorineural hearing loss.
- Auditory neuropathy spectrum disorder: it is a hearing loss occurring when sound enters the ear normally but due to damage to the inner ear or the auditory nerve, the sound is not organized in a way that the brain can understand.

In this thesis, we will focus on sensorineural hearing loss. The causes of this hearing loss can be of different types. It can be caused by acoustic trauma (intense, violent sounds), toxins and certain ototoxic antibiotics (gentamycin, family of aminoglycosides), infection of the inner ear, or it can occur later with age, which is called presbycusis [25].

Among all forms of hearing loss, an important point is to distinguish between congenital deaf and post-lingual deaf. In the first case, the person is born with a hearing loss, which means that she is deaf before learning to speak, whereas post-lingual deafness occurs after the person has learned to speak. The main difference between these two categories is directly related to the brain and its organization, as certain areas of the brain, such as those dedicated to language for example, may be allocated to other functions for a person with a pre-lingual hearing loss. This thesis is based on post-lingual deaf subjects.

2.3 Cochlear Implant

The Cochlear Implant (CI) is a solution for people who are profoundly deaf or severely hard of hearing. As for those people the cochlea is hardly damaged, the cochlear implant will consist of a system put in place in the cochlea, that will electrically stimulate the auditory nerve to give the person some auditory sensations and allow her to hear.

The cochlear implant consists of an internal and an external part. The external part is placed behind the ear while the internal is placed under the skin during surgery under general anesthesia [54]. As we can see in Fig 2.8, the external part is composed of a microphone, which picks up the sounds from the environment,

and an audio processor converting sound waves into numerical signals [55] [56]. The information is then transferred through the coil to the implant into the skin, and to the electrode array placed into the cochlea that will stimulate the auditory nerve [57].

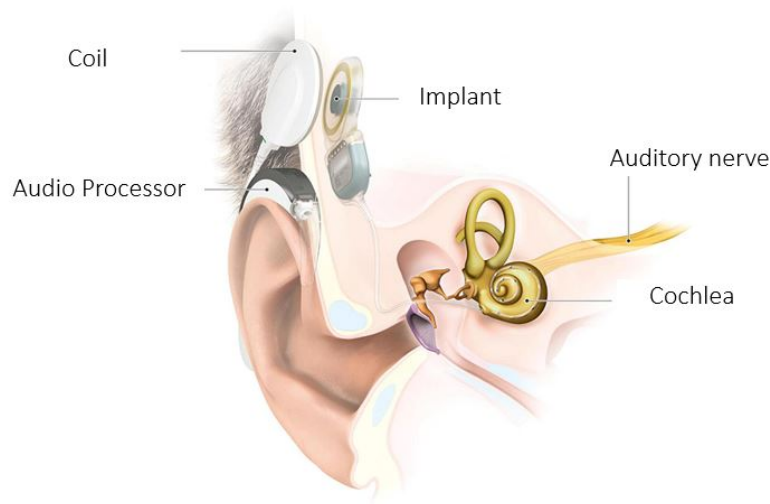


Figure 2.8: Cochlear implant, composed of an external and internal part. The external part contains a microphone and an audio processor converting sound waves into numerical signals, a battery, and a coil. The internal part is implanted during surgery and contains the implants that will electrically stimulate the fibers of the auditory nerve through electrodes placed in the cochlea. Adapted from [54].

Nevertheless, a cochlear implant is not a miracle solution. The cochlear implant recreates sounds, meaning that sounds perceived by the patients are not real sounds, but artificial sounds and voices. It implies that the patient has also to follow an intensive reeducation to be used to those new apparel and learn to recognize and interpret those new sounds [58].

It could also be a risk from the surgical procedure, and the patient could suffer of minor complications after the implantation, such as transient chorda tympani syndrome, vertigo/dizziness, or more major complications such as wound infection or permanent chorda tympani syndrome [59]. Moreover, there are many factors contributing to the results, such as the cause of deafness, age at onset of deafness, duration of hearing deprivation, residual hearing, or duration of hearing aid use [60]. It could also happen that the cochlear implant does not work properly. Devices failure can be soft, leading to a deterioration in the patient auditory performance or to new symptoms associated with the port of the implant [61]. Furthermore, they can be harder, meaning that the outer and inner parts of the cochlea implant are completely disconnected, so the device is failing entirely [61].

In the worst case, reimplantation following revision surgery could be required. And last but not least, it is a very expensive solution. In Belgium, with health insurance funds one can be reimbursed for one implant, but not for a second one, which cost around 22 000€ [62].

The purpose of this thesis is therefore to predict the outcome of a cochlear implant on a deaf person, to avoid, in the case of predicting failure, a lot of expensive and exhausting steps for the patient.

2.4 Audiometry

A sound is a sonorous vibration of the air. The frequency of a sound is defined as the number of cycles by seconds, in Hertz (Hz). In humans, the audible range is between 20 to 20 000 Hz with a particular range, between 100 to 3500 Hz, essential to the understanding of the language [25].

To control and measure the auditory acuity of a patient, we use a set of methods called audiometry. An audiometry exam tests the ability to hear sounds. They exist several types of audiometry tests, the two most commonly used being pure-tone audiometry and speech audiometry.

Pure-tone audiometry consists of delivering pure tones of specific frequencies to the subject through either headphones (i.e. air conduction) or a vibrator pressed against the mastoid portion of the temporal bone (i.e. bone conduction). The goal is to identify the lowest level at which the subject can detect each frequency, also known as the threshold [63]. Air Conduction (AC) hearing thresholds are usually measured for tonal stimuli at the range of frequencies from 0.125 kHz to 8 kHz while bone conduction hearing thresholds are mostly measured in a range of thresholds from 0.25 to 4 kHz [64]. Results are presented on a diagram frequency (Hz)/intensity (dB HL) called an audiogram. Note that the unit used here for the intensity is the dB Hearing Loss (HL) and not dB Sound Pressure Level (SPL). The latter describes the local pressure deviation caused by a sound wave and it is the reference unit for calibration signals or earing equipment. The dB HL is a derivative of the dB SPL and is used to measure how loud we can hear a sound [65]. In the audiogram, we will therefore use the dB HL unit.

One can interpret an audiogram in the following way. If the results are in the grey area on the top of the graphs represented in Fig. 2.9, the audition is normal. The result present in the white area, at the bottom, represents on the contrary hearing loss. And the higher the score (the lower on the graph) the deeper the hearing loss [66].

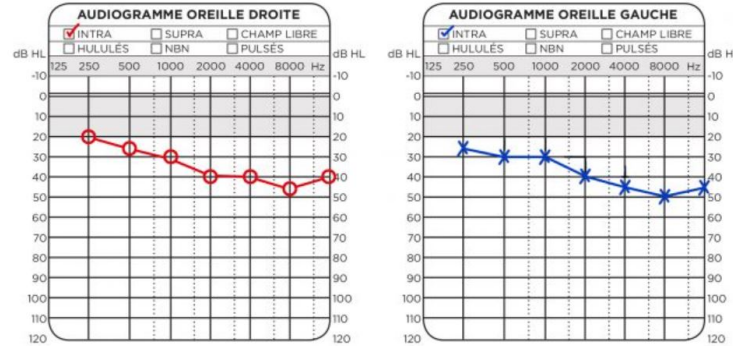


Figure 2.9: Example of audiogram for the right ear (red) and left ear (blue). The grey area represents the "normal" hearing area. The lower we go down in the white part of the diagram, the more severe the hearing loss. Results are presented in dB HL. From [67].

Speech audiometry or speech reception threshold is an audiometry test measuring the intensity at which the patients can correctly reproduce fifty percent of the words they hear. The goal of this test is to reflect the hearing sensitivity for speech [63]. Those tests are performed with different lists of words with different levels of difficulty. For example, the Fournier list (in French) uses words with close tones. The most significant phonetic test (in French) is the list of Lafon cochlear (short words) because it does not involve mental substitution and linguistic knowledge. It, therefore, makes it possible to assess the real social and linguistic handicaps that the hearing impaired may experience [67].

Another important test to measure the auditory performance is the Categories of Auditory Performance (CAP). It is used to measure speech perception performance by measuring supraliminal performance, which reflects everyday auditory performance in a more realistic way. It consists of a system evaluating auditory perceptual skills on a scale of 0 to 7, with 0 indicating no awareness of environmental sounds and 7 indicating the ability to use the telephone with a familiar speaker [68].

Finally, the Speech Intelligibility Rating (SIR) is employed to gauge speech intelligibility based on natural, spontaneous speech. It comprises five performance categories spanning from "words that are not recognizable in spoken language" to "connected speech that is intelligible to all listeners" [69].

2.5 Previous studies

This section presents a non-exhaustive overview of the results of previous research on the use of DTI for the analysis of the white matter pathways related to audition and language in patients with sensorineural hearing loss. The populations studied, methods used, areas, and metrics investigated will be summarised.

2.5.1 Comparative studies

Here we group together studies that have decided to tackle this problem by comparing two or more populations. Some compare deaf people with controls, others compare prelingual deaf people with postlingual deaf people.

Y. Li et al. compared white matter structure among three groups: congenitally deaf individuals, acquired deaf individuals, and age-matched hearing controls [44]. They used diffusion tensor imaging and tract-based spatial statistics to investigate modifications in the structural connections. They focus on the variation of the FA metrics in three cluster areas: the right superior temporal gyrus, the left Heschl's gyrus, and the splenium of the corpus callosum. They found significantly reduced FA values in the right superior temporal gyrus for both congenitally and acquired deaf patients compared to hearing controls. Moreover, they found decreased FA values in the left Heschl's gyrus for the congenitally deaf compared to the hearing group. Finally, they discovered reduced FA values in the right superior temporal gyrus and in the splenium of the corpus callosum for congenitally deaf compared to acquired deaf patients [44].

J. Kim and colleagues performed a comparative study of white matter integrity in patients with prelingual and postlingual deafness [42]. They realized a tract-based statistical analysis of diffusion tensor anisotropy in eight areas: the superior temporal gyrus, the Heschl gyrus (right and left), the right temporal white matter, the right internal capsule, the right thalamus, and the body and splenium of the corpus callosum. They found significantly lower FA values in the right superior temporal gyrus, bilateral temporal white matter, and the genu and anterior body of the corpus callosum for postlingual deaf patients compared to prelingual deaf patients.

A study realized by E. Kim. et al tried to investigate changes in white matter integrity and white matter anatomical connectivity in both early- and late-onset deaf groups compared with hearing group [43]. They use a tract-based spatial statistics method implemented on FSL software and calculated FA, AD, and RD. They found no notable changes between the control group and the early-onset

deaf group. However, they found specific alterations in white matter areas for the late-onset deaf group compared to the control group. These alterations were characterized by decreased FA and increased RD. The affected regions included the corpus callosum, posterior and superior corona radiata, internal capsule, posterior thalamic radiation, superior longitudinal fasciculus, and tapetum of the right hemisphere. Additionally, increased RD was observed in the right external capsule, fornix, and cerebral peduncle. However, there were no significant differences in axial diffusivity AD between the late-onset deaf group and the hearing group [43].

2.5.2 DTI and Cochlear Implantation

Other studies focus on understanding the outcome of cochlear implantation through DTI techniques [70].

Huang et al. conducted a prospective study on patients with congenitally prelingual deafness who underwent a DTI scan before receiving a cochlear implant [71]. They separated the patients into two groups according to their CAP score. Patients with a postoperative CAP score ≥ 6 were classified as a good outcome group and those with a postoperative CAP score < 6 as a poor outcome group. Then, they realized a diffusion tensor analysis on six ROIs of the brain: the trapezoid body, the superior olivary nucleus, the inferior colliculus, the auditory radiation, and the white matter of Heschl's gyrus. They calculated the FA and MD values for those six areas. They found that the FA values were significantly higher in the good outcome group for the six ROIs. There was no significant difference between the two groups in terms of MD values. Additionally, regression analysis revealed a positive correlation between FA measures in all six regions of interest and CAP scores [71].

Y. Chang. et al studied patients with pre-lingual deafness by using a voxel-wise analysis of diffusion tensor imaging [72]. Similarly to Huang et al., they separated patients into two groups according to their CAP score. Here, they investigated the FA values at the medial geniculate nucleus, the Broca's area, the genu part of the corpus callosum, and the auditory tract near the primary auditory cortex. Moreover, they performed a correlation analysis between the FA values of the ROIs and CAP scores, open sentence, and open word scores. They discovered that subjects with good outcomes demonstrated notably higher FA values in various brain regions, such as Broca's area, the genu of the corpus callosum, and the auditory tract when compared to those with poor outcomes. Furthermore, correlation analyses between FA values and measures of CAP scores, open sentence scores, and open word scores revealed strong associations specifically in the medial geniculate nucleus, Broca's area, the genu of the corpus callosum, and the auditory tract [72].

A study realized by C. Wu et al. also used this CAP classification strategy to highlight WM differences between good and bad CI outcomes [73]. Moreover, they also compared control patients to patients suffering from prelingually sensorineural hearing loss. They investigate FA values through diffusion tensor imaging for two brain areas: the superior temporal gyrus and auditory radiation. They found significantly higher FA value in the auditory radiation in the good outcome group compared to the bad outcome. Moreover, correlation analyses at 12 months post-operation revealed strong correlations between the FA and CAP scores in the auditory radiation. Finally, they found decreased FA value in the deaf group compared to the hearing group for the auditory radiation and the superior temporal gyrus [73].

2.5.3 Overview and limitations

The table below, Table 2.1, resumes the results of the research presented in this section. Although this summary is not exhaustive, it includes articles considered relevant to this thesis. However, it is important to bear in mind that plenty of studies have examined deafness and cochlear implants via tractography, but very few in the same way. Moreover, only two of these studies presented here included another metric in addition to FA. It is for the simple reason that this metric is almost the only one used in research. In addition, very few studies correlate diffusion measurements with various objective and subjective hearing tests [70]. Finally, the subject of this study has not often been discussed, despite the fact that postlingually deaf people represent the majority of the deaf population [54].

Table 2.1: Studies overview. Abbreviations: STGr = Superior Temporal Gyrus right ; HG = Heschl's gyrus ; SCC = Splenium of the Corpus Callosum; GCC = Genu of the Corpus Callosum; BCC = Body of the Corpus Callosum; IC = Internal Capsule; SLF = Superior Longitudinal Fasciculus; CRp = Posterior Corona Radiate; CRs = Superior corona Radiate ; CP = Cerebral Peduncle , AR : Auditory Radiation

References	Results
Comparative studies	
Li et al. [44] <i>Acquired deaf vs Control</i> <i>Congenitally deaf vs Control</i> <i>Congenitally deaf vs Acquired deaf</i>	↘ FA in STGr ↘ FA in STGr and in HG ↘ FA rSTG and SCC
J. Kim et al. [42] <i>Prelingual vs postlingual</i>	↘ FA in STGr, temporal WM, GCC and BCC
E. Kim et al. [43] <i>Late-onset deaf vs control</i>	↘ FA and ↗ RD in the CC, CRp, CRs, IC, posterior thalamic radiation, SLF, and tapetum right ↗ RD in the right external capsule, fornix, and CP
DTI and CI	
Huang et al. [71] <i>Poor vs good CI outcome</i> <i>Correlation analysis</i>	↘ FA in trapezoid body, superior olivary nucleus, inferior colliculus, AR and HG - FA correlated with CAP score in trapezoid body, superior olivary nucleus, inferior colliculus, AR, and HG
Chang et al. [72] <i>Poor vs good CI outcome</i> <i>Correlation analysis</i>	↘ FA in Brocas area, GCC, AR - FA correlated with CAP scores, open sentence scores, and open word scores in the geniculate nucleus, Brocas area, GCC, and AR
Wu et al. [73] <i>Poor vs good CI outcome</i> <i>Correlation analysis</i> <i>Congenitally deaf vs Control</i>	↘ FA in AR - FA correlated with CAP score in AR ↘ FA in AR and STG

Part II

Tractography of auditory and language pathway

Chapter 3

Methods

The aim of this master thesis is to predict the outcome of cochlear implantation in adults with postlingual deafness via tractography of auditory and language pathway. To this end, two strategies will be investigated, with the same starting point.

The first is inspired by the method used by Chang Y et al. in their retrospective study "Voxel-wise analysis of diffusion tensor imaging for clinical outcome of cochlear implantation" [72]. They separated the subjects into two categories according to their CAP score. Those with a CAP score of 6 or more corresponded to good outcomes and those with a CAP score smaller than 6 to poor results. We will follow this strategy but divide the patients into two groups according to their corrected Average Word Recognition Score (AWRS) 6 months after implantation, as this criterion is more objective. Therefore, those with a corrected AWRS greater than 0.5 will be considered great results and "good outcome", and those with a corrected AWRS equal to zero as unsatisfactory results and "bad outcome". The objective here is to try to determine what would be the significant parameters that would be linked to a better recovery.

The second strategy consists of investigating the possible correlations between the results of the different audiometric tests performed 6 months post-operative and the values obtained after the analysis of the tracts (pre-operative DTI metrics). Before either of these strategies can be carried out, certain steps must be taken: the selection of the areas to be tracked, the performance of tractograms on these areas for all patients, and the collection of data and metrics resulting from the tractograms.

These two methods and the different steps will be explained in more detail in the following sections.

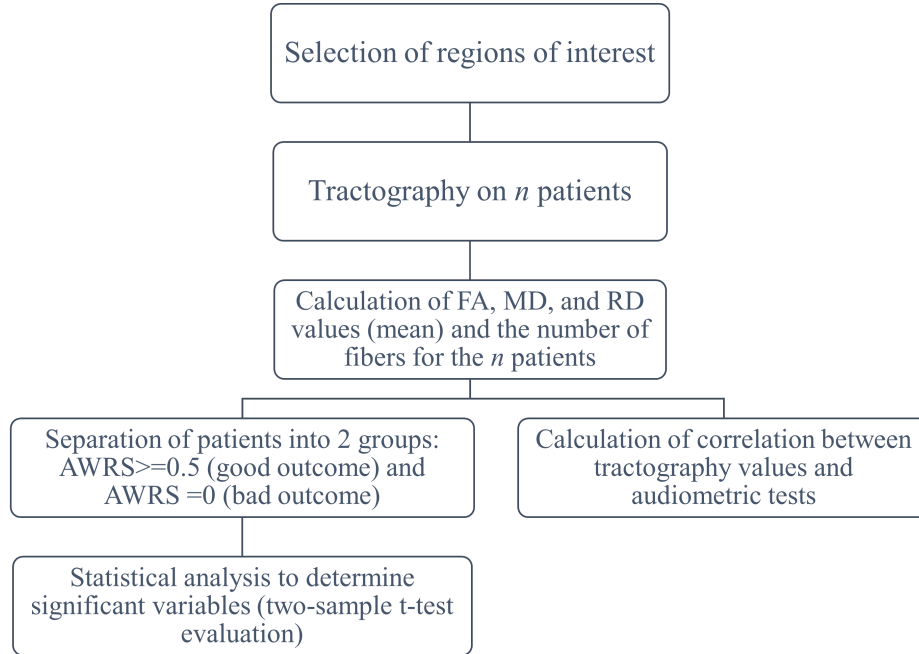


Figure 3.1: Diagram of key steps and strategies.

3.1 Data

The dataset used in this thesis was acquired in Saint-Luc Hospital (Brussels) on a 3T Siemens MRI scanner in the framework of the Ph.D. thesis of Dr. Anais Gregoire. To perform tractography, single-shell DTI images (resolution 128x128x56x65, TE = 74 [ms], TR = 9000 [ms]) were exploited. During the acquisition, 64 non-collinear diffusion gradients were applied with a b-value of 800 s/mm², and a separate set of images with no diffusion weighting (b = 0 s/mm²) was also obtained.

Note that data used here were already exploited by L. Anizet and A. Doyen for their master thesis "Biomarker identification for vertigo through human connectome analysis" [74]. Therefore, the pre-processing of those data was already performed. This preprocessing pipeline consisted of brain extraction, reslicing, denoising, artifact suppression, distortion correction, motion modeling, and bias field correction to prepare brain imaging data for analysis [74].

The original data set includes 85 deaf patients who underwent pre-operative MRI for the purpose of cochlear implant surgery. For this thesis, the data set was reduced to 53 patients. Data from patients who were prelingually deaf, had other brain problems, or whose DTI maps were missing or not adequately acquired were discarded from this study.

In addition to the medical data from the MRI, behavioral data (age of patients, duration of hearing aid use, type of implant,...) was gathered by Dr. Anaïs Grégoire for each patient and can be found on Appendix A. Moreover, data from audiometric tests performed pre-implant and 3, 6, and 12 months post-implant were collected. It should be noted that those data are not available for all patients. The audiometric tests performed were: air conduction (AC) at 0.5, 1, 2, and 4 kHz, Word Recognition Score (WRS) at 65 dB, and average word score recognition (AWRS), CAP, SIR, and DEWA. The latter is an audiovisual integration test devised by Justine Wathour et Naïma Deggouj, which measures the ability of deaf people to understand a situation with or without visual support (e.g. lip reading). A score out of 15 is given (converted here between 0 and 1), depending on the percentage of understanding of the person. Note that the AWRS is calculated by averaging the results obtained at 40 dB (soft voice), 55 dB (moderate voice), and 70 dB (loud voice). Moreover, different lists of words were used (see section 2.4). Easier lists have sometimes been used in order to encourage patients who had more difficulties, or simply because they were not able to achieve results with a difficult list. As patients were not all tested on the same difficulty level, this difference may distort the final results. Dr. Anaïs Grégoire has therefore proposed a correction of these tests, calculated on the basis of patients who had been tested on several lists (see Appendix A).

In the following sections of this thesis, we will focus more on the DEWA, AWRS (corrected), and CAP tests. Those tests are more relevant when discussing cochlear implants because they reveal more about the ability to understand language and words, and not just hearing sounds. Nevertheless, all audiometric tests listed above were performed and their results can be found in Appendix F.

3.2 Tractograms realisation

For this study, eight white matter areas involved in auditory processing and language were selected for investigation: the left arcuate fasciculus (AF), the genu, body, and splenium of the corpus callosum (CC), the left and right uncinate fasciculus (UF) and the left and right inferior fronto-occipital fasciculus (IFOF). The tractography of those regions is presented in Figs. 3.7, 3.8, 3.9 and 3.10.

3.2.1 Whole brain tractography

The production of tractograms is performed in several steps. The first step consists of building a whole-brain tractogram with tractography algorithms. In this thesis, we will use probabilistic tractography algorithms inspired from Dipy [75]. To use these algorithms, we need three key elements: diffusion data, seed points, and a mask in which the tracks are computed. As some parameters can be tuned,

it is important to understand their role and impact on the final tract. Firstly, we can tune the density of seed points. Increasing this number will increase the number of tracts starting from each voxel. For example, if the seed density is set to 2, 8 tracts will start from one voxel, and if it is set to 3, 27 tracts will start from the voxel. Other parameters that can be tuned are the FA threshold and the Generalized Fractional Anisotropy (GFA). For a probabilistic algorithm, those parameters were set respectively to 0.6 and 0.35. Finally, the maximum angle between two tractography steps and the step size for tracking should be determined. For those regions, the maximum angle was set to 15° and the step size to 1 mm.

As the tracked regions have specific sizes and shapes, seed density has been modified to fit each region as closely as possible. These values are listed in the table below:

Table 3.1: Seed density for the eight ROIs.

ROIs	Seed density
AF	2
CC Genu	2
CC Body	2
CC Splenium	2
UF left	1
UF right	1
IFOF left	3
IFOF right	3

Once the parameters have been selected, the probabilistic algorithms will create a whole brain tractogram of each patient's brain. An example of a whole brain is shown in Fig.3.2 with different seed densities. One can easily see that brain 3.2b, which has twice the seed density of brain 3.2a seems denser and more crowded.

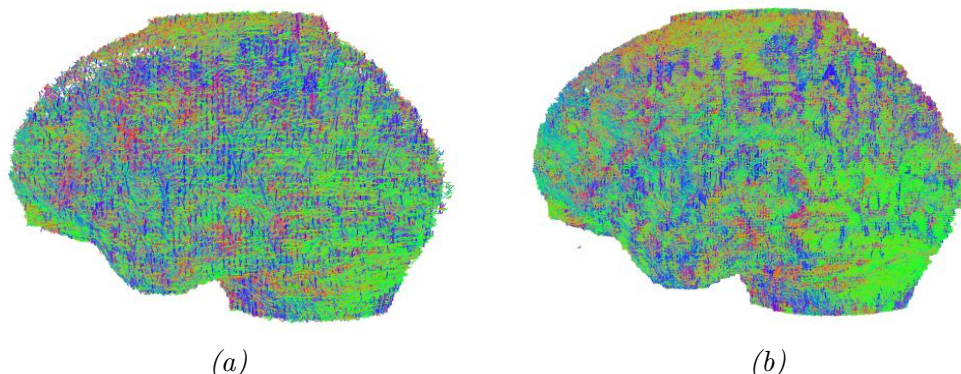


Figure 3.2: Whole brain tractography, (a) with a seed density of 1.5 and (b) with a seed density of 3. Generated on TrackVis [23].

3.2.2 ROIs registration

To perform tractography in these chosen areas, one needs to define specific regions of the brain as Region Of Interest (ROI). The second step, therefore, consists of generating specific ROI for each patient. Two atlases are used for that purpose. The first one is a probabilistic atlas provided by the Harvard Center for Morphometric Analysis, covering grey matter areas of the brain. It corresponds to 48 cortical and 21 subcortical structural areas [76]. The five lobes of the brain were also selected (insula, occipital, parietal, temporal, and frontal). These could be downloaded from FSL and come from the Research Imaging Center [77].

The second atlas covers the white matter of the brain and consists of 42 probabilistic tract maps published by Warrington et al. These maps were designed in the framework of their study on standardized protocols for automated tractography in the human and macaque brain [78].

It should be noted that the atlases provided are standardized and registered in the Montreal Neurological Institute (MNI) space, a standard space defined by averaging several human brains [79]. As each patient has a unique brain, it is important to register the ROI from the atlases in a new space, the "patient space", which corresponds to each patient and which will allow the correct delineation of the regions to be investigated. This registration was made through functions inspired by Dipy tutorial and takes place in two steps [80]. Firstly, a function takes a static volume (here a DTI map) and a moving volume (here an FSL HCP1065 standard-space FA map, shown in Fig. 3.3) as argument and returns a transform operation sending the moving volume to the static volume space. Afterward, a second function applies the transformation on the atlas map to reproduce it in the patient space.

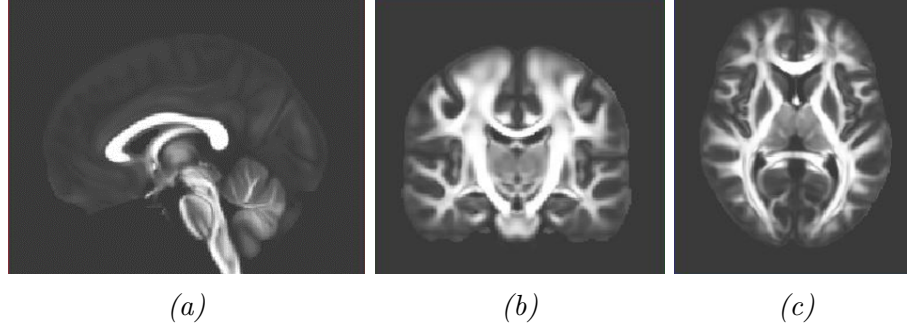


Figure 3.3: FSL HCP1065 standard-space FA map. Sagittal **(a)**, coronal **(b)** and axial view **(c)** of the brain.

Fig.3.4 shows those maps at different steps. On the left, the static volume, specific to each patient, and on the right, the moving volume, from the MNI space. The overlay on those two maps can be observed in the middle, in Fig. 3.4b. Registration is therefore important because these two maps do not overlap perfectly. In summary, this allows us to move from the initial MNI space to the patient space while maintaining the characteristics of each ROI. Fig. 3.5 also shows a map of the brain where the arcuate fasciculus, shown in green, can be seen before and after the registration step.



Figure 3.4: Maps registration steps. **(a)** represents the DTI static volume map, **(c)** the FSL HCP 1065 moving volume and **(b)** shows the overlay of the static and moving volume.

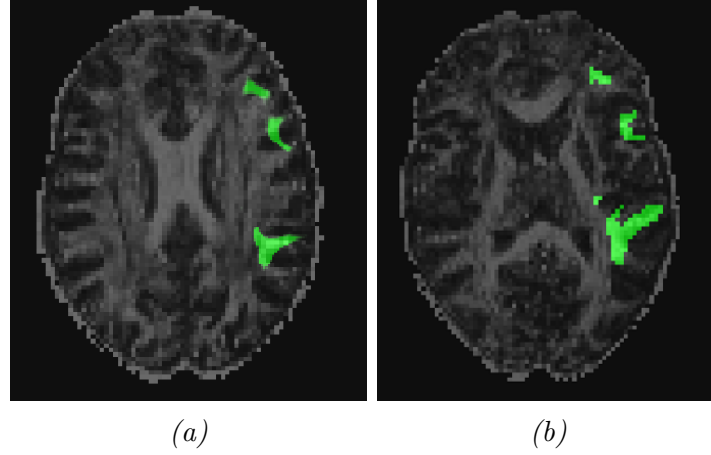


Figure 3.5: Comparison between a nonregistered and registered region of the brain. The green part shows the AF (a) not registered and (b) registered on a FA map with a threshold of 0.5.

When this step is performed, the ROIs selected will be created in 3D for each patient. An example of an arcuate fasciculus generated for a patient is represented in Fig. 3.6 and visualized through the TrackVis program [23]. Note that if the majority of ROIs were created under a threshold of 0.5, some specific regions were created under a different threshold (8, 50, 90...) to refine the areas to be studied. Details about the threshold kept for each ROI are included in Annexe B.

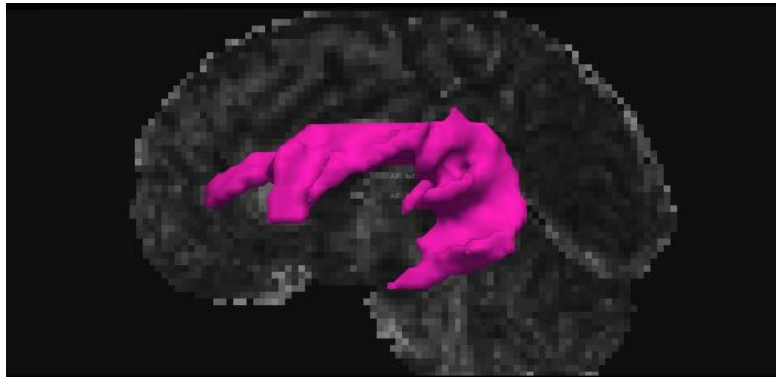


Figure 3.6: Arcuate Fasciculus of a patient after registration with a threshold of 0.5, illustrated in TrackVis [23].

3.2.3 ROIs tractography

The last step is the realization of the final tracts for the eight regions we want to study. We are interested in the white matter fibers that make up each of these regions, and only these regions. To make accurate tractograms, it is now necessary to link certain ROIs together, i.e. to connect the regions where these fibers pass and to remove those where anatomically they do not pass. This is done through logical combinations: OR/AND/NOT [81]. The OR-operator returns fibers that pass through one or two ROIs, whereas the AND-operator is more restrictive and only returns fibers that pass through both ROIs, while the NOT-operator eliminates fibers that enter a particular ROI [81].

These eight regions were then consciously formed by combinations of ROIs, based on their anatomical shapes and definitions [82, 83, 84]. Regions kept or rejected for each tracked zone are listed in Annexe B. Once a tract is validated, it is generalized for the n patients. The figures below show the resulting track for an example patient.

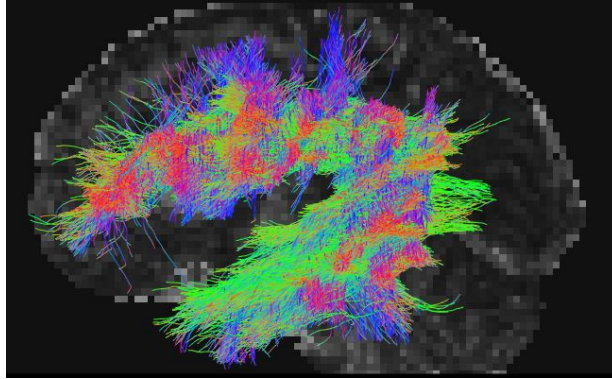


Figure 3.7: Tractography of the left arcuate fasciculus. Generated on TrackVis [23].

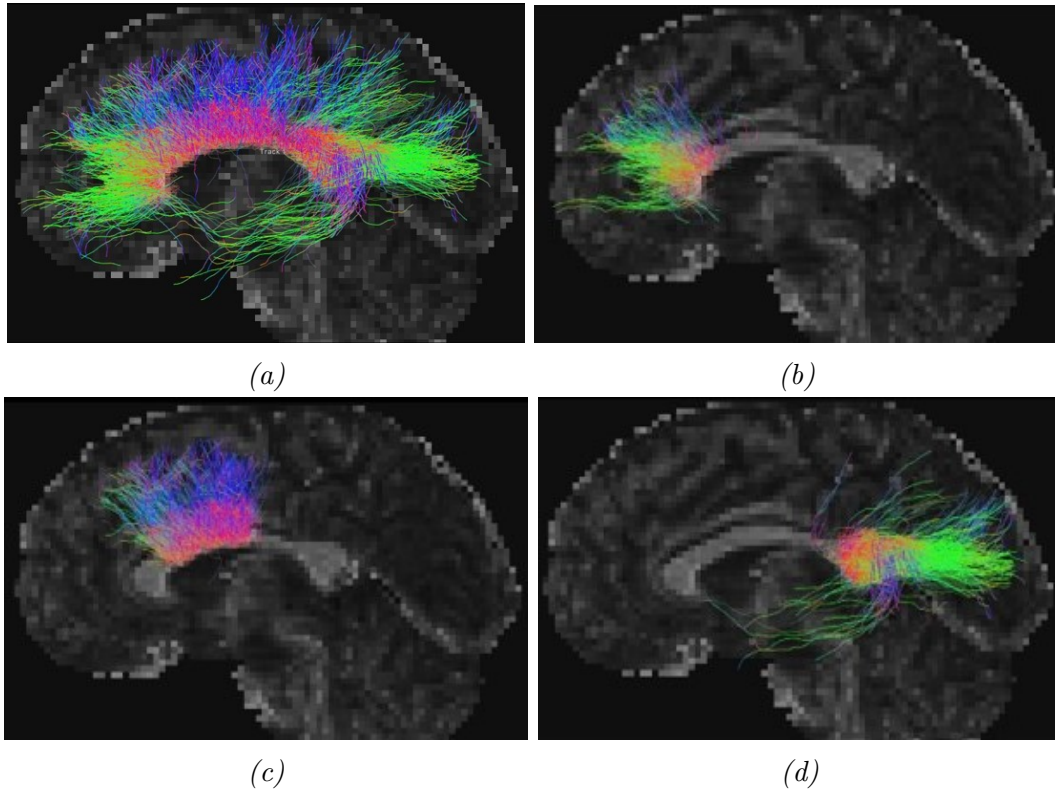


Figure 3.8: Tractography of the Corpus callosum **(a)**, the genu of the CC **(b)**, the body of the CC **(c)** and the splenium of the CC **(d)**. Generated on TrackVis [23].

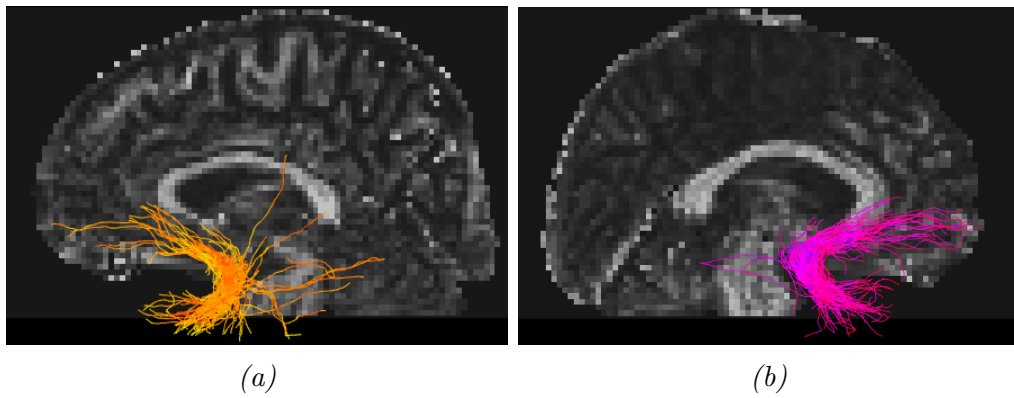


Figure 3.9: Tractography of the left uncinate fasciculus **(a)**, and the right uncinate fasciculus **(b)**. Generated on TrackVis [23].

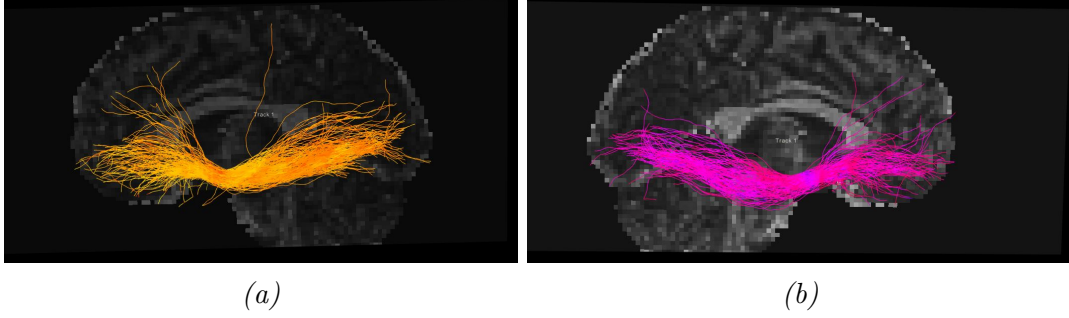


Figure 3.10: Tractography of the left IFOF (**a**), and the right IFOF (**b**). Generated on TrackVis [23].

3.2.4 Data extraction from tractograms

Once the tracts are completed for each region and for each patient, the values of interest can now be extracted. Here we will extract the mean value of the FA, MD, and RD metrics as well as the number of streamlines (or tract count). All these metrics were weighted by the streamline density. Fig. 3.11 shows examples of density maps for the arcuate fasciculus and the corpus callosum.

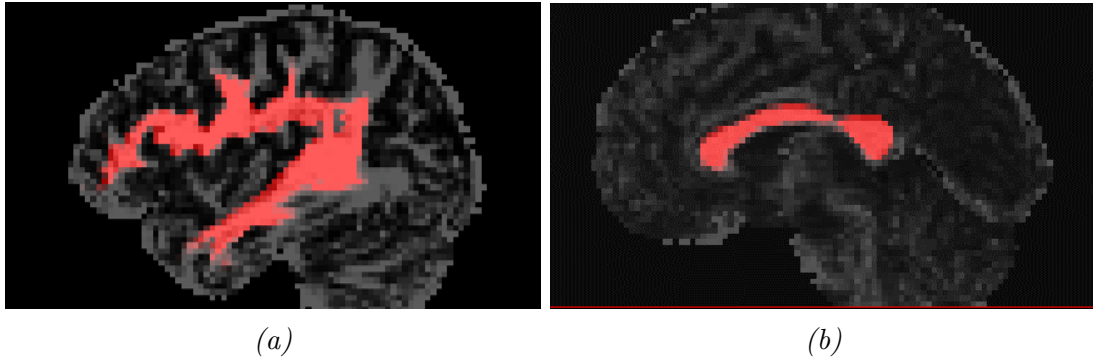


Figure 3.11: Density maps of the Arcuate Fasciculus (**a**), and the corpus callosum (**b**). The red part shows the fiber density for each respective part of the brain on an FA map.

3.3 Statistical analysis and correlation

For the first part of the analyses, patients were separated into two groups according to their 6 months post-operative corrected AWRS score: good outcome ($\text{AWRS} \geq 0.5$) and bad outcome ($\text{AWRS} = 0$). Two-sample t-tests were evaluated to highlight the possible significant variables between those two groups. A variable was considered significant and discriminating between those two groups if its associated p-value was under 0.05.

For the second part, a correlation analysis was performed between audiometric tests (AWSR, DEWA, and CAP) and values, i.e. streamline count, and mean of FA, MD, and RD. Pearson correlation was used to determine correlations among FAs, MDs, RDs, and audiometric scores. The correlation coefficient and associated p-values were calculated. Correlations were performed for two situations:

- correlations between audiometric results (AWRS, DEWA, CAP) tested 6 months after implantation and data from pre-implant MRI metrics.
- correlations between the difference in behavioral data (DEWA, CAP) between time 2 (six months after the implantation) and time 1 (before implantation) and data from pre-implant MRI metrics. The purpose here is to see if diffusion metrics correlate with behavioral improvement. Note that for this case we do not look at the AWRS as it is difficult to compare because of the different word lists used before and after the implantation.

Correlations were also performed between pre-implantation behavioral data and pre-implant MRI metrics to ensure that the correlations that would be observed after implantation are not in fact already present from the beginning. In the event that this is observed, this data will simply not be taken into account in the analysis of the results.

Since several statistical tests are performed, a certain fraction of the p-values obtained may be false positives. Bonferroni correction to multiple tests was therefore applied [85]. While the significance level is usually $\alpha = 0.05$, it will become:

$$\alpha = \frac{0.05}{\text{Number of tests performed}}. \quad (3.1)$$

In addition, one can observe that the age of the patients had a significant correlation ($p < 0.05$) with the preoperative DTI values (see Fig 3.12).

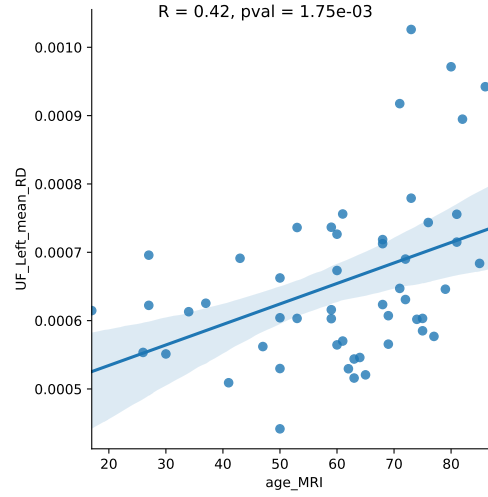


Figure 3.12: Correlation between the age and the metrics values from MRI preoperative. The plot shows a positive and significant correlation ($p = 0.00175$) between the age of the patients when surgery and the mean RD of the left uncinate fasciculus.

This means that this parameter can influence the results. The correlation analysis, therefore, had to be corrected for this covariate. This is done through partial correlation [86]. Partial correlation is a correlation technique measuring the effect of the combination of two variables, x and y , after removing the effect on one or more controlling variables Z [86]. Here, the controlling variable we want to remove the effect is the age of the patient at the time of the implantation. To obtain the partial correlation, we first compute the residuals eX and eY through linear regression of x with Z and y with Z , respectively, and then calculate the correlation between these residuals [87]. An example of this correction can be seen in Fig. 3.13.

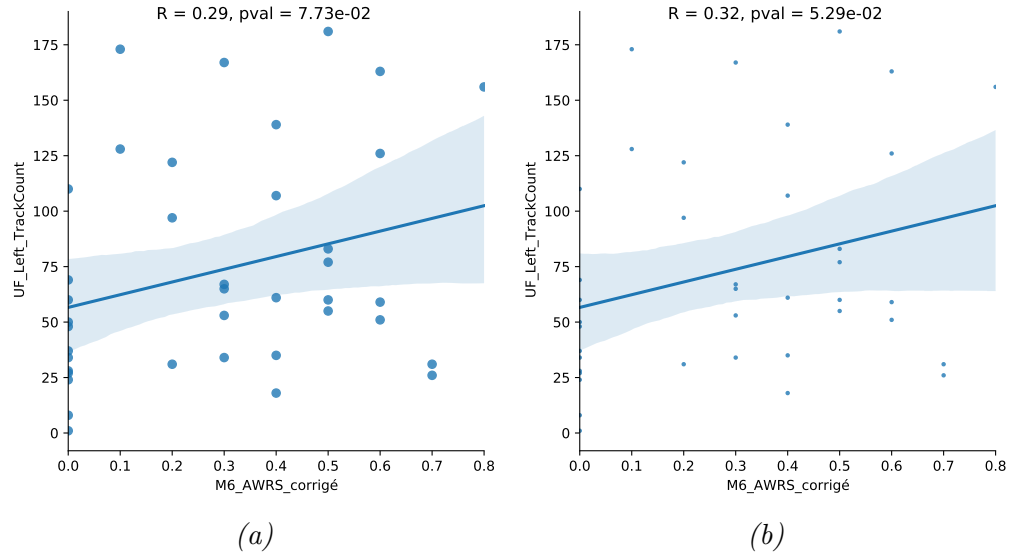


Figure 3.13: Example of corrected correlation for age between the corrected AWRS six months after implantation and the track count of the left UF. Plot (a) shows the correlation without correction and plot (b) with correction.

Chapter 4

Results

This section gathers the results obtained for the two strategies presented above. They are divided into two parts, corresponding to the two strategies explored here: the AWRS and DTI metric analysis, and the correlation analysis between DTI metrics and audiometric tests.

4.1 AWRS and DTI metrics analysis

The first strategy was to separate the patient cohort into two groups regarding their corrected AWRS score. As a reminder, the AWRS score is a test demonstrating the ability of a patient to understand and repeat words. The final score corresponds to the percentage of words correctly repeated, here converted into a score between 0 and 1. As in the behavioral data gathering by Dr. Anaïs Grégoire and presented in Appendix A, patients with an AWRS score ≥ 0.5 were classified into the good outcome group (great results), and patients with an AWRS equal to 0 were classified into the bad outcome group (unsatisfactory results). The aim was to determine the significant parameters that would be linked to a better recovery. A two-sample t-test was therefore applied, as explained in the previous chapter, and results with p-values under 0.05 were kept.

As the corrected AWRS score was not recorded for every patient, the analysis was performed on 39 patients. Among them, 12 had an AWRS score ≥ 0.5 , and 12 had an AWRS score =0. Their demographic and clinical data can be found in Table. 4.1.

Table 4.1: Patient demographic and clinical data

	Good outcome (N=12)	Bad outcome (N=12)	P-value
Age	55.66+-16.93	58.83+-21.79	0.707 (>0.05)
Time HA	16.66 +- 13.31	19.33 +- 14.99	0.663 (>0.05)
AWRS	0.59 +-0.095	0	<0.0001

Two-sample t-test evaluation analysis found significantly lower MD values in good-outcome patients compared to poor-outcome patients for seven brain areas: left AF ($p=0.010$), genu ($p=0.042$), body ($p=0.027$) and splenium ($p=0.047$) of the corpus callosum, left UF ($p=0.013$), right IFOF ($p=0.045$) and left IFOF ($p=0.027$). It also shows significantly lower RD values in good-outcome patients compared to poor-outcome for the left UF ($p=0.022$). The three most significant results are presented in Fig. 4.1, others can be found in Appendix D.1.

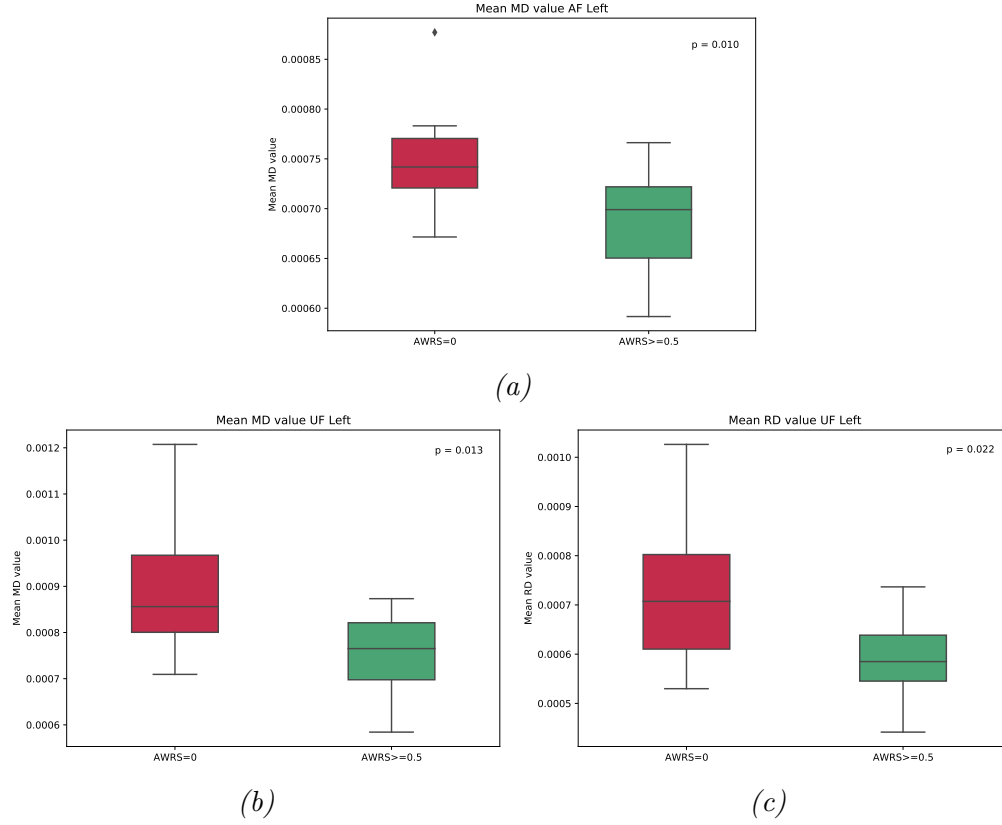


Figure 4.1: Two sample t -test evaluation analysis shows significantly higher values of MD in the bad-outcome group (red box-plots) compared to the good-outcome group (green box-plots) for the left AF (a), and the left UF (b), as well as higher values of RD in the bad-outcome group (red box-plots) compared to the good-outcome group (green box-plots) for the left UF(c).

Moreover, it shows a significantly higher number of streamlines in good-outcome patients compared to poor-outcome patients in the splenium of the CC ($p=0.043$), the left UF ($p=0.013$), and the right IFOF ($p=0.044$).

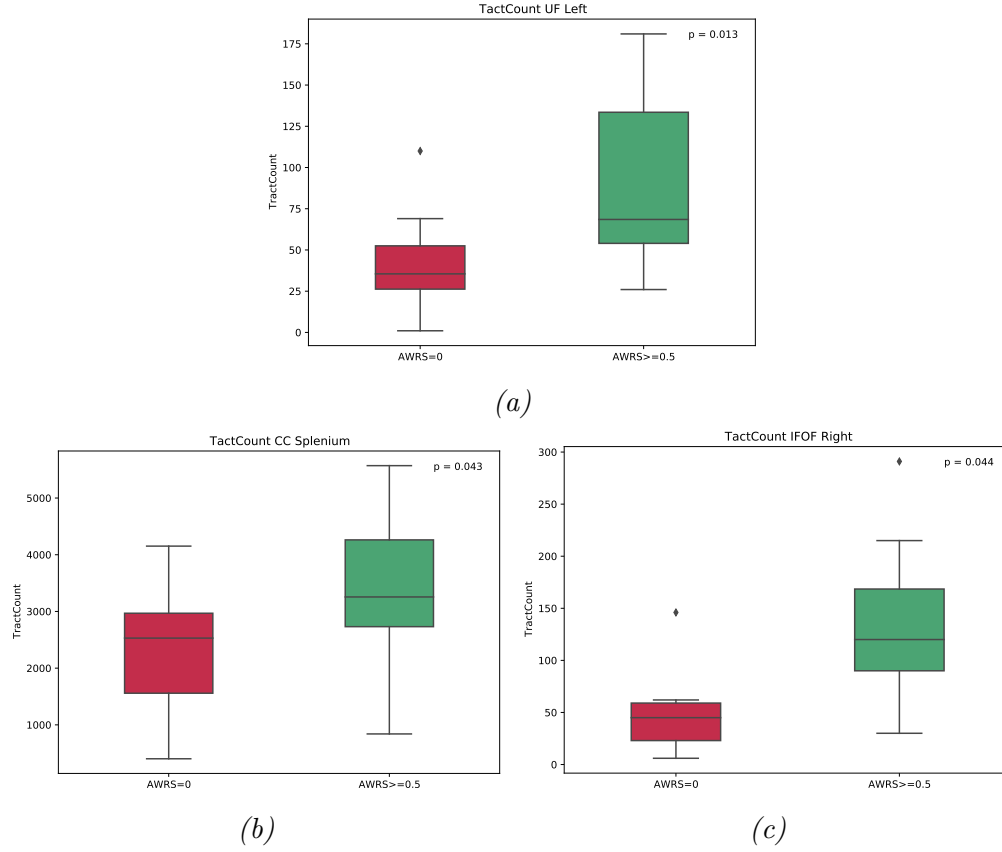


Figure 4.2: Two sample t -test evaluation analysis shows a significantly higher number of streamlines in the good-outcome group (green box-plots) compared to the bad-outcome group (red box-plots) for the left UF (a), the splenium of the corpus callosum (b) and the right IFOF (c).

4.2 Correlation analysis

The results are shown for correlation between pre-operative diffusion metrics and behavioral data 6 months post-implantation and for correlation between pre-operative diffusion metrics and behavioral improvement.

Only significant correlations were kept and presented in the following subsections. For the correlation between diffusion metrics and behavioral data 6 months post-implantation (CAP score, corrected AWRS, and DEWA), statistical analysis reveals about twenty results with a p -value <0.05 . To avoid false positives, Bonferroni correction to multiple tests was therefore applied.

As three tests were performed, the new level of significance became :

$$\alpha = \frac{0.05}{\text{Number of tests performed}} = \frac{0.05}{3} = 0.0166. \quad (4.1)$$

Four results remain significant and will therefore be presented in the following sections. The other results are available in Appendix E.

For the correlations between diffusion metrics and behavioral improvement, five results were highlighted with a $p\text{-value} < 0.05$. Results are presented area by area.

4.2.1 Arcuate Fasciculus

Statistical analysis of the left AF shows a significant negative correlation between the corrected AWRS and the mean MD values ($p = 0.0131$). It can therefore be observed in Fig. 4.3 that the lower the pre-operative mean MD value, the higher the corrected AWRS 6 months post-implantation.

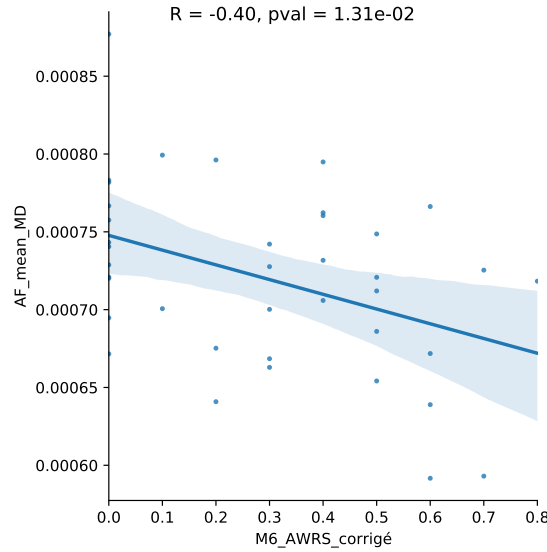


Figure 4.3: The correlations between the average word recognition score (AWRS) corrected and the mean MD of the left AF. The line is the result of a linear regression.

4.2.2 CC Body

Statistical analysis of the body of the CC reveals a significant negative correlation between the DEWA score 6 months post-implantation and the pre-implantation

mean MD ($p=0.0154$). Moreover, it shows two highly significant negative correlations between the improvement of the DEWA score and two metrics of pre-implantation DTI: the mean MD ($p=0.00403$) and the mean RD ($p=0.00529$). As can be seen in Fig. 4.4, the DEWA score and the evolution of the DEWA score increase when the pre-operative MD and RD of the body decrease.

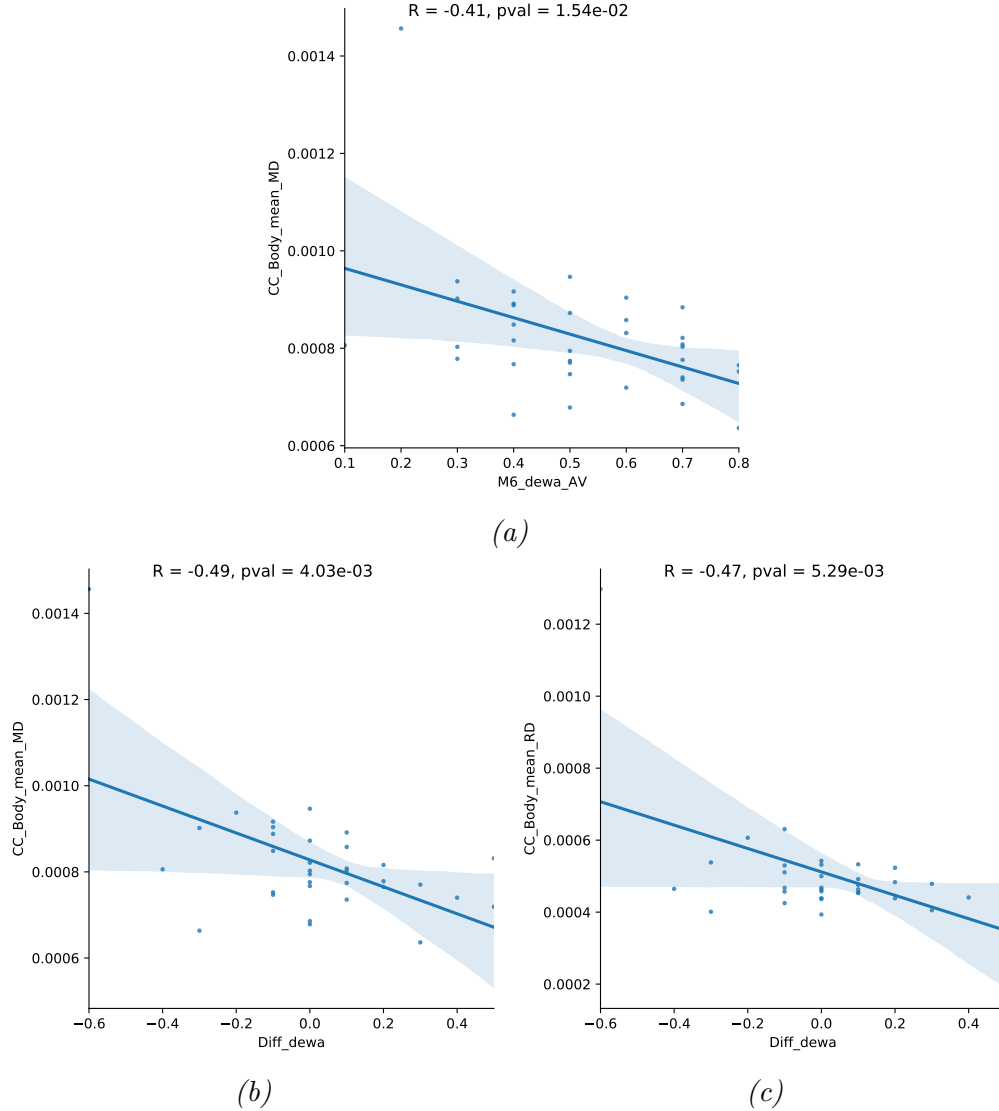


Figure 4.4: The correlation between the DEWA score post-operative and the mean MD (a) as well as the correlations between the evolution of the DEWA score and the mean MD (b), and RD (c) of the body of the CC. The lines are the result of a linear regression.

4.2.3 CC Genu

The analysis of the genu of the corpus callosum reveals one significant positive correlation between the improvement of the CAP score and the mean RD values ($p=0.0369$). The more the pre-operative RD metric of the patient increases, the more he increases his CAP score between the post- and pre-operative times.

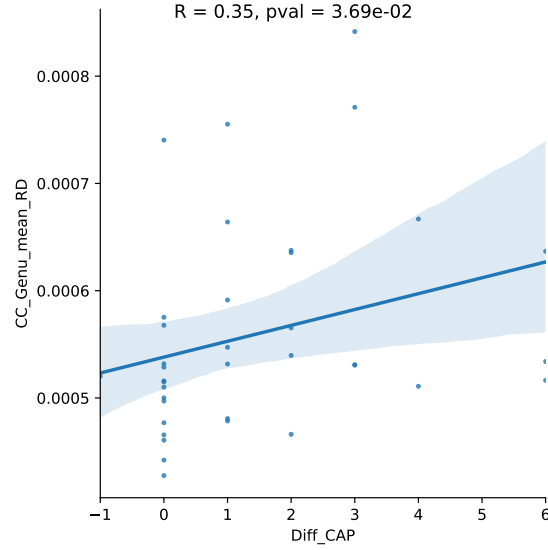


Figure 4.5: The correlations between the improvement of the CAP score and the mean RD values for the genu of the CC. The line is the result of a linear regression.

4.2.4 CC Splenium

The analysis of the splenium of the corpus callosum reveals one significant negative correlation between the improvement of the DEWA score and the mean MD values ($p=0.0471$). The more the pre-operative MD metric of the patient decreases, the more he increases his DEWA score between the post- and pre-operative times.

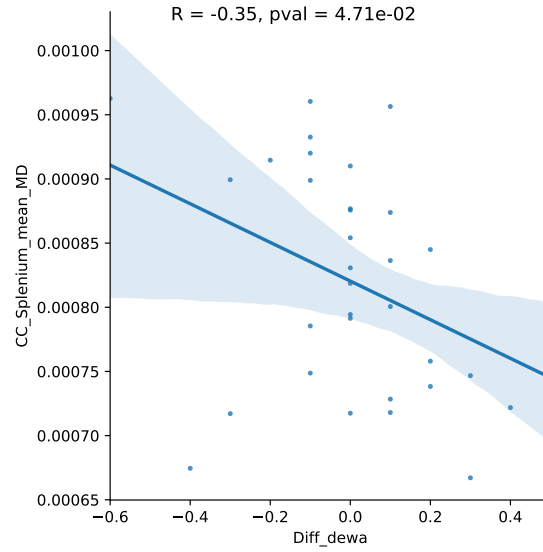


Figure 4.6: The correlations between the improvement of the DEWA score and the mean MD values for the splenium of the CC. The line is the result of a linear regression.

4.2.5 UF left

Statistical analysis of the left uncinate fasciculus reveals several significant results. Firstly, it shows a significant positive correlation between the DEWA score 6 months post-implantation and the pre-operative FA ($p=0.00431$) of the left UF. A significant negative correlation between the DEWA score 6 months post-implantation and the pre-operative RD ($p=0.00272$) was also found but has to be discarded from the results as the DEWA score pre-operative was already correlated with the pre-operative RD ($p=0.0189$).

Moreover, correlation analysis also reveals a significant negative correlation between the 6 months post-implantation corrected AWRS and the pre-operative mean MD values ($p=0.0146$). The lower the MD value, the higher the AWRS score.

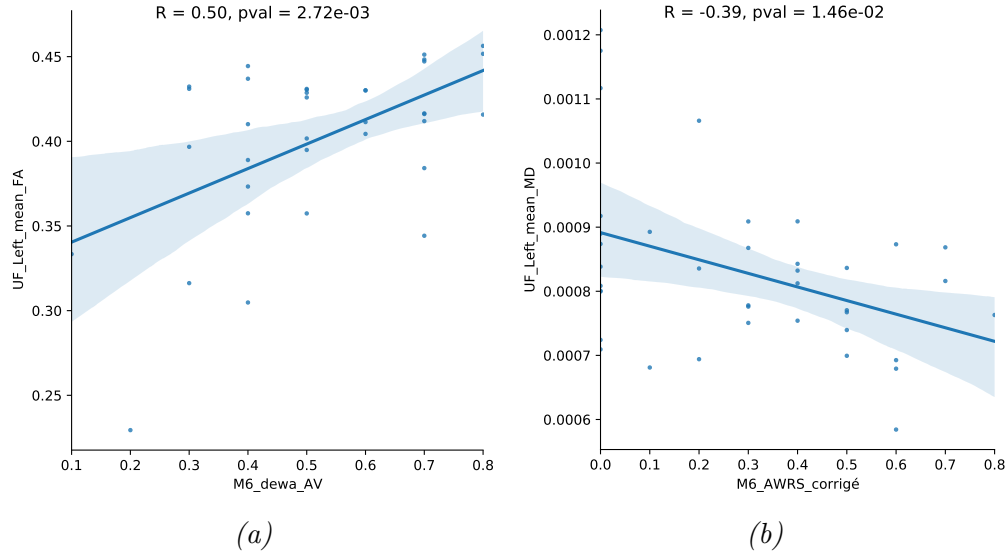


Figure 4.7: The correlation between the DEWA and the mean FA values (a) and the correlation between the corrected AWRS and the mean MD values (b) of the left UF. The lines are the result of a linear regression.

4.2.6 IFOF right

The analysis of the right IFOF shows a significant negative correlation between the evolution of the DEWA score and the pre-operative mean FA values ($p=0.0331$).

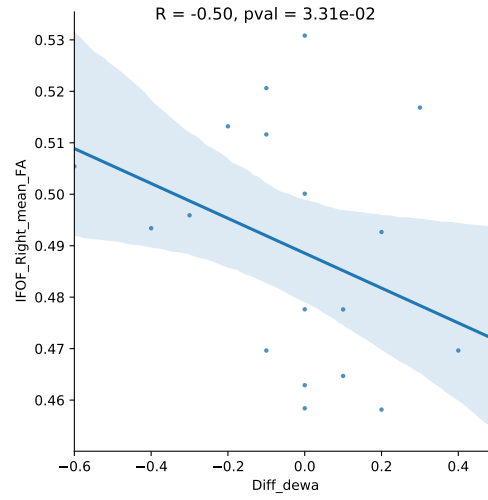


Figure 4.8: The correlations between the evolution of the DEWA score and the mean FA of the right IFOF. The line is the result of a linear regression.

Chapter 5

Discussion

In this chapter, results obtained for the AWRS and DTI metrics analysis and for the correlation analysis will be discussed. A critical analysis and interpretation of the results of each strategy will be independently performed before making a general analysis. The outcomes will also be compared with those of previous studies. Finally, the limitations of this study and possible improvements will be discussed.

5.1 Results interpretation

The theme of the application of DTI to the auditory system and cochlear implants is quite binary in the literature, focusing largely on the presence or absence of a difference in diffusion measures between deaf patients and controls. Furthermore, very few studies correlate diffusion measurements with various objective and subjective hearing tests [70]. Moreover, the vast majority of papers focus on prelingual patients. In this thesis, however, we are studying adults with postlingual deafness. The topic of this study has not been addressed a lot, despite the fact that postlingual deaf people represent the majority of the deaf population [54]. It, therefore, explains the scarcity of literature available on this topic to make direct comparisons. This study aims to fill this gap by exploring an area that has been little explored until now and by providing new insights and using innovative methodologies.

5.1.1 Justification of the choices made for the strategies

To predict the outcome of cochlear implantation in adults with postlingual deafness, we used two strategies.

The first was to separate the patients into two groups according to their post-implantation corrected AWRS. Those with a score above 0.5 were considered "good

outcome" and those with a score of zero were considered "bad outcome". Two-sample t-tests were then performed to identify significant parameters that could discriminate between the two groups. This strategy is based on the retrospective study of Y.Chang et al, "Voxel-Wise Analysis of Diffusion Tensor Imaging for Clinical Outcome of Cochlear Implantation" [72]. The AWRS parameter was chosen as the classifier parameter because it is less subjective than the CAP. For the latter, no test is actually carried out. Indeed, the doctor simply asks the patient how he identifies his hearing on a scale from 0 to 7. In the AWRS, on the contrary, doctors test the patient's ability to repeat words heard at different frequencies (soft, loud, and moderate voice). Moreover, the classification used here is based on behavioral data provided by Dr. Anaïs Grégoire, who classified the patients into three groups according to their AWRS. In addition to the two categories listed above, she defines a third group corresponding to scores between 0.1 and 0.4, referred to as "correct" results. The choice was therefore made to include only the two groups with the most extreme scores, in order to highlight the most significant differences between those who have regained their hearing the most and those who have regained it the least.

The second one consisted on calculated the correlation between the values obtained from pre-implant DTI and the score or improvement score of audiometric tests realized 6 months after the surgery.

In both cases, the set of DTI parameters tested were the mean values of three metrics of DTI, FA, MD, and RD as well as the number of streamlines for the eight brain regions: the AF, the genu, body, and splenium of the corpus callosum, the right and left UF as well as the right and left IFOF.

We extracted those three metrics, FA, MD, and RD as they can characterize the integrity of the WM, and therefore the integrity of the communication channels of the brain. The better the quality of these pathways, the more likely it is that neural exchanges will be effective. Although FA is the most commonly studied metric in the literature, it is also important to take into account other metrics, such as MD or RD, as they may together give more information on white matter integrity. Indeed, using FA, AD, and RD values as standalone biomarkers of cerebral white matter microstructure may lead to incorrect conclusions [88]. According to C.R Figley et al., MD would be the strongest and most interpretable metrics for drawing reverse inferences about the underlying tissue characteristics and theoretically the more robust to multiple fiber populations and/or complex fiber geometries [88]. We, therefore, decide to calculate MD as the first metric. FA was then calculated, as it is the most widely used metric in the literature, which could allow more comparisons to be made. Finally, a third metric, RD, was also taken into account in this study for two reasons. Firstly, because it is one of the most studied metrics in this field after FA, and secondly, because combined with RD and FA, it provides

a more complete characterization of fibers bundle integrity. Previous studies and research highlighted that high FA values and low RD and MD values represent good integrity of white matter [11]. Conversely, low FA, high MD, and high RD may indicate significant alteration of the bundles, suggesting pathological changes or lesions. The AD metric was not taken into account in this study as it is not a widely used measure in this field of research. Moreover, we decided to concentrate our research on the analysis of MD, RD, and FA, in order to have a broad field of research without spreading ourselves too thinly.

Finally, the last variable was the tract count or streamline count. The number of streamlines can also be used to characterize the microstructure of the WM, as a measure of the density or integrity. A high number of streamlines between auditory regions may indicate optimal connectivity and transmission of auditory signals in the brain.

The results will first be interpreted by strategy, before having a more general discussion including a comparison to previous studies on similar topics.

5.1.2 AWRS and DTI metrics analysis

Statistical analysis of the AWRS and DTI strategy found significantly higher MD values in poor-outcome patients compared to good-outcome patients for the left AF, the genu, body, and splenium of the corpus callosum, the left UF, the right IFOF, and the left IFOF as well as higher RD values in poor-outcome patients compared to good-outcome for the left UF. Significant RD values were only found for UF left and no significant FA values were reported. The combination of high MD alongside normal RD and FA for the poor-outcome patients suggests an elevated overall water diffusion within the tissue, without significant changes in myelin integrity or fiber coherence. This heightened diffusion, indicated by high MD values, implies increased tissue diffusivity in all directions. It may be indicative of increased extracellular space, changes in tissue composition, or conditions with cellular loss. Moreover, for the left UF, the combination of high MD and RD values with normal FA for the poor-outcome patients can suggest potential alterations in the tissue microenvironment or myelin integrity. These results, therefore, suggest worse axonal integrity in poor-outcome patients than in good-outcome patients in those 7 areas of interest. Patients with postlingual deafness would therefore tend to have better outcomes in AWRS 6 months after CI implantation if their pre-operative MRI shows a relatively well-preserved white matter at brain areas associated with language and auditory functions.

Moreover, it also reveals a significantly higher number of streamlines in good-outcome patients compared to poor-outcome in the left UF, the right IFOF, and the splenium of the corpus callosum. Patients with more fibers in these areas on pre-operative MRI would have better outcomes 6 months after surgery. Since a

large number of streamlines suggests a large number of connections, it can be assumed that these connections may play an important role in the transmission of auditory and language information.

5.1.3 Correlation analysis

Statistical analysis of this second strategy shows significant negative correlations between AWRS and MD values for the AF and the left UF. A high word recognition score 6 months after implantation, therefore, correlates with a low pre-op MD value. Again, a low preoperative MD value in areas of the brain related to language and audition (as the left arcuate and uncinate fasciculus), would suggest well-preserved axonal integrity, and therefore better hearing outcomes 6 months after implantation.

Moreover, statistical analysis reveals a significant negative correlation between the DEWA and the MD values of the body of the corpus callosum as well as a significant positive correlation between the DEWA and the FA values of the left UF. A high post-operative score of DEWA is therefore linked to high pre-operative FA values and low pre-operative MD values. The association of low MD with normal FA and RD indicates restricted water diffusion within the tissue while maintaining normal fiber coherence and myelin integrity. Moreover, high FA values combine with normal MD and RD values suggest a healthy and structurally intact white matter in the left UF. These results again suggest that strong connectivity and integrity within the white matter (high FA and low MD) in brain areas such as the left UF or the CC would be crucial parameters to ensure qualitative post-implantation results.

This analysis also highlights a significant negative correlation between the improvement of the DEWA score and the MD and RD values of the body of the CC, the MD values of the splenium of the CC, and the FA values of the right IFOF. The parameter "improvement" is calculated by making the difference between the DEWA score post and pre-operative. The higher the difference, the more likely it is that the patient has improved their audio-visual integration skills. The results here, therefore, show a high improvement in the DEWA score correlates with low MD and RD values. Combined with normal FA values, these measurements evoke restricted diffusion of water into the tissue while maintaining normal fiber coherence and myelin integrity. Therefore, well-preserved pre-implant white matter integrity (low MD and RD) in areas of the brain such as the corpus callosum (body and splenium) would allow the patient to improve more after the operation in terms of audio-visual integration. Nevertheless, there is also a result that does

not go in the same direction as all those found previously. The negative correlation between the improvement of the DeWa and the FA values of the right IFOF suggests that a high improvement score would be linked to a low FA value. This result is in opposition with the previous one, as the analysis between DTI metrics and AWRS found that a better audition recovery was associated with reduced MD. Moreover, the study of F. T. Husain et al., found a decrease in FA values in the right IFOF for the hearing loss group compared to normal hearing controls [89]. However, a low FA value is not necessarily synonymous with poor WM integrity. Certain elements such as crossed fibers, fiber crimping, or an increased fiber radius can also influence this variable. In this case, low FA values associated with normal RD and MD values can indicate reduced coherence or disruption in the fiber tracts without significant changes in overall diffusion or myelin integrity. As F. T. Husain's study only calculated the FA metric, we cannot conclude with certainty that the low FA values found here for the right IFOF are synonymous with degraded white matter.

Finally, it found a significant positive correlation between the improvement of the CAP score and the RD values of the genu of the CC. An improvement of the CAP score would therefore be correlated with a high RD value. High RD values combine with normal FA and MD values indicate an increase in diffusion perpendicular to the nerve fibers, while overall diffusion and fiber coherence remain relatively intact. It also suggests a potential alteration in the myelin sheath, which can be associated with demyelination or damage to the myelin fibers. This result is in opposition with the previous ones, as it suggests that an altered white matter of the genu of the CC would allow the patients to improve their CAP score after implantation. Two hypotheses could explain this result. Firstly, this could be due to residual hearing as N. M. Armstrong et al. found that better hearing was associated with reduced FA and normal MD at the level of the genu of the corpus callosum [45]. This remains a plausible lead, but it needs to be verified by other research, as it is at odds with the results found in the analysis between DTI metrics and AWRS. The latter found that a better audition recovery was associated with reduced MD. The second hypothesis that could explain this result is that the variable "improvement of the CAP" could be inadequate. In addition to being a fairly subjective test, the CAP does not seem to be the best predictor of hearing ability. A closer look at the pre-cochlear implant data shows that patients with CAP scores of 7 (the highest score) have an AWRS with a hearing aid equal to those with CAP scores of five, four, three, or even zero. Furthermore, patients who had a high CAP score (6, 7) before cochlear implantation generally kept this score after implantation. The "improvement" factor is therefore biased by the fact that almost forty percent of patients neither improve nor worsen their results, but just stagnate at a correct score.

5.1.4 General interpretation

These two strategies lead to the same findings: patients who have kept a better WM integrity (high FA and low MD and RD values) in the brain areas related to audition and language (arcuate and uncinate fasciculus, corpus callosum, and IFOF) before the cochlear implant have better results 6 months after the operation, for the word recognition tests (AWRS) and the audio-visual integration tests (DEWA). The preservation of the axonal integrity of those areas would therefore be linked to a better recovery audition in adults suffering from post-lingual deafness.

Arcuate Fasciculus

The preservation of the WM integrity of the left AF is in both cases a factor that has been put forward as important to obtain better results in terms of word recognition (AWRS), due to low MD values associated with high AWRS. This seems consistent given that the arcuate fasciculus links Wernicke's and Broca's areas, (i.e., the area of comprehension of the language, and that of the production of the language [25]) and that this test requires the patient to understand the words he has just heard in order to repeat them. The arcuate fasciculus has also been shown to play an important role in language comprehension and production, in particular, naming and fluency [90]. Moreover, the left arcuate fasciculus, in particular, is thought to play a role in phonemic awareness and language perception [8].

Uncinate Fasciculus

The left uncinate fasciculus is an area of the brain that shows similar results in both experiments. Low MD, RD, and high FA values preoperative (and thus well-preserved white matter integrity) of the left UF are related to positive results of AWRS and DEWA 6 months after implantation. Research suggested that the UF could play a role in language as well as episodic and auditory memory, social-emotional processing, semantic associations, and sound recognitions [39, 40]. Moreover, it had been shown that reduced white matter integrity in the uncinate fasciculus is associated with reduced auditory memory [91]. N. M. Armstrong et al. have also demonstrated that poorer central auditory processing was associated with MD increases and FA declines in the uncinate fasciculus [45]. Moreover, R. Qi. et al. also found that RD values were increased in the uncinate fasciculus in patients with sensorineural hearing loss compared to hearing control [92]. A well-preserved WM integrity of the left UF is therefore another important parameter to take into account to ensure great CI outcomes.

Corpus Callosum

For this thesis, three parts of the corpus callosum were studied: the genu, the body, and the splenium. In both strategies, a high WM integrity of the CC (low MD and RD) is associated with great results post-cochlear implantation (AWRS, DEWA, and improvement of the DEWA). An exception is the correlation between the genu of the CC and the improvement of the CAP score, discussed previously.

The corpus callosum is a structure that connects the two cerebral hemispheres, allowing an incalculable number of information exchanges through its numerous connections. While simple tasks are easily performed by a single hemisphere, complex tasks require inter-hemispheric cooperation [93]. Furthermore, as the brain undergoes aging, the significance of this collaboration increases, particularly in tasks that necessitate bilateral activation, whereas younger brains predominantly rely on a single hemisphere to perform those tasks [94].

These results presented here echo those found in the literature. Previous studies about pre-lingual deaf children had shown higher FA values in areas of the brain associated with language and auditory function as well as the genu of the corpus callosum, suggesting that maintaining its microstructural integrity is important [72]. Moreover, W. Miao et al. show that low FA and high RD values in the splenium of the corpus callosum are linked to poorer hearing ability [95]. Furthermore, a comparative study between prelingual and postlingual deaf patients also shows a decrease of WM integrity in prelingual compared to post-lingual patients for the genu, body, and splenium of the CC [42]. Additionally, N. M. Armstrong and colleagues discovered a consistent link between diminished peripheral auditory abilities and an increase in MD in the body of the corpus callosum [45]. A study of white matter connectivity also finds a decrease of FA values in the splenium of the corpus callosum for congenitally deaf individuals compared to acquired deaf patients [44]. Moreover, E. Kim et al. found a decreased FA and increased RD in several white matter areas including the genu, body, and splenium of the corpus callosum for late-onset deaf subjects compared to the hearing group [43]. In addition, Qi et al. also discovered lower FA values in the splenium, the body, and genu of the CC, as well as higher RD values in the genu and the body of the CC in patients with sensorineural hearing loss, compared to hearing controls [92]. It seems therefore evident that the integrity of the white matter of the corpus callosum, whether genu, body, or splenium, plays an important role in the hearing and language process. Moreover, the microstructure of the CC seems also altered by the onset of post-lingual deafness, especially if it occurs at an advanced age. In summary, the conservation of the microstructure of the CC would therefore lead to better audition recovery post-implantation for these post-lingual patients, allowing

a significant improvement in audio-visual integration, a complex task requiring the activation of both hemispheres.

Inferior Fronto-Occipital Fasciculus

The results obtained on the IFOF converge in the same direction as the previous ones, except the one from the correlation between the right IFOF and the improvement of the DEWA, discussed previously. We found that increased MD values and a low number of streamlines (pre-op data) are associated with low word recognition scores (AWRS) 6 months after the intervention. Previous studies also demonstrated that poorer peripheral auditory function was linked to higher MD values in the inferior fronto-occipital fasciculus [45]. Moreover, Qi et al. also found that RD values were increased in the IFOF in patients with sensorineural hearing loss compared to hearing control [92]. This sizable white matter pathway could play a role in the integration of auditory and visual association areas with the prefrontal cortex [45]. Again, preserving the integrity of the white matter, here in the IFOF, appears to be important for obtaining satisfactory CI outcomes.

In summary, well-preserved preoperative white matter in the left arcuate fasciculus, the left uncinate fasciculus, the corpus callosum (genu, body, and splenium), and the right and left IFOF would be a key factor to better post-cochlear implant audition recovery. The summary map below (Fig. 5.1) shows the brain areas significantly linked to post-implant results in terms of speech perception (AWRS) and audio-visual integration (DEWA).

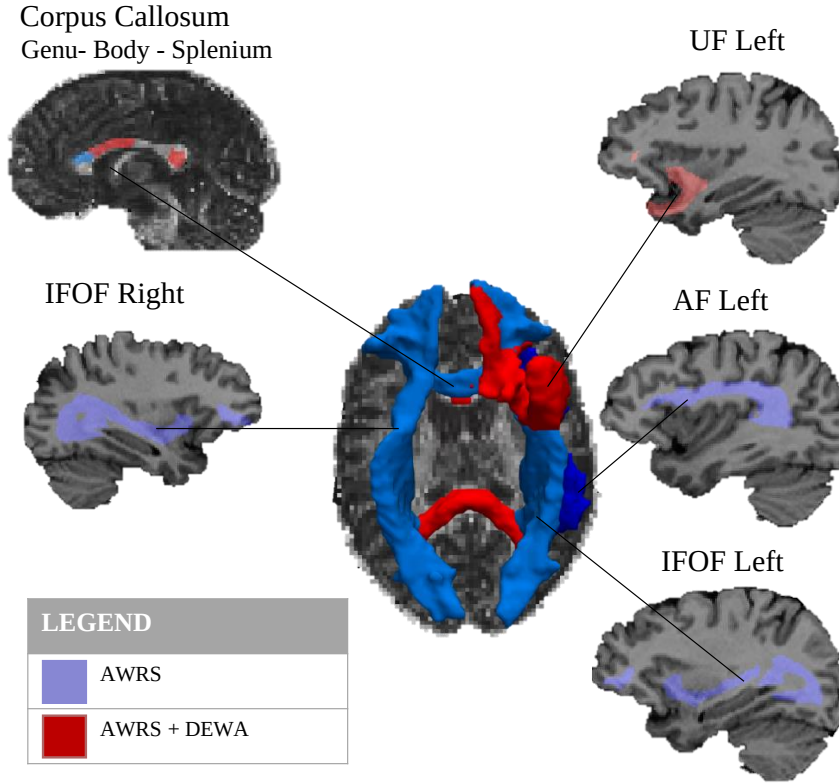


Figure 5.1: Summary map. Illustration of areas of the brain that have significant links with post-cochlear implant outcomes. The integrity of the WM of the genu of the CC, the right and left IFOF, and the AF (represented in blue) has an influence on post-cochlear implant speech perception (AWRS). The integrity of the WM of the left UF, as well as the body and splenium of the CC (represented in red), has an influence on post-cochlear implant speech perception (AWRS) and audio-visual integrity (DEWA).

5.2 Limitations

This section discusses the remaining limitations of this thesis, which are essential to be aware of when interpreting the results developed in the previous section.

Data

First of all, as mentioned above, this study was carried out on about 60 patients. Nevertheless, pre- and post-cochlear implantation behavioral data were not acquired for all patients. To ensure consistent results, it would be preferable in the future to perform these studies on a constant number of patients, and for whom all behavioral data are present.

Furthermore, with regard to the behavioral data, some tests should be interpreted with care. Although the AWRS was corrected by Dr. Anaïs Grégoire to overcome the problem that not all patients were tested with the same word lists, this correction may be subject to interpretation. To obtain unequivocal results for this test, it would be best to evaluate all patients on the same word list. However, this is not always so easy in practice. Therefore, it would be wise to use and test this correction in other studies, in order to validate it.

In this thesis, the results were corrected for the age of the patients, as there was significant evidence that this value was correlated with the results. Hearing aid wearing time was also tested and found to have no significant impact. However, other parameters could have been tested to ensure that they did not influence the final results, such as the implanted side, gender, or implant type.

Tractography

The tractography part also has some limitations. Firstly, for a more complete study, it would be wise to extend the number of ROIs. Regions such as the cingulum, the fornix, or even those more specifically related to the central auditory pathways, such as acoustic radiation, could be analyzed. However, the latter remains tricky to track. This is due in particular to the problem of fiber crossing, the small size of some subcortical fibers, and these anatomical characteristics [96]. In addition, it would also be interesting to investigate other brain regions that are not directly related to hearing or language, in order to ensure the significance of the results. If the same patterns are found in all brain areas, this reduces the interest in looking at specific regions related to language and audition. Conversely, if these areas are not found to be significant in the results, then this adds to the interest in studying those related to language and audition.

Furthermore, although the tracts were made as accurately as possible, DTI, tractography techniques, and algorithms used here still present intrinsic limitations. They were presented earlier in this thesis and must be taken into account when interpreting the results.

The corpus callosum could also have been segmented into five zones and performed more accurately. The corpus callosum tracts performed here were based on an atlas that did not explicitly include CC-related ROIs. The latter was generated by linking the two hemispheres and removing inappropriate areas for each part (body, genu, and splenium). Using another atlas and other tools (such as WMQL based on FreeSurfer segmentation for example [97]) might be a interesting idea to refine this region to be tracked.

Finally, the interpretation of the streamline count must also be done with care. It is necessary to differentiate this streamline count from the number of "real" fibers, as the number of fibers reconstructed between two regions may be different because of the actual anatomy, the performance of the tracking algorithm, or the parameters chosen during tractography.

Relevance with the literature

As mentioned above, a number of studies have investigated deafness and cochlear implants via tractography, but very few in the same way. The variability in the ROIs, the types of hearing loss studied, the diffusion indices measured, the audiometric tests assessed, and the statistical methods used make it difficult to compare results between them.

Finally, it should be noted that the interpretation of diffusion metrics (FA, MD, RD) remains subjective. It is still difficult to understand precisely the impact of these metrics variations on medical studies other than those concerning diseases clinically diagnosed as impacting the white matter (demyelinating diseases, ischemia, and tumor infiltration) [98]. Other imaging modalities or measures may also be necessary to confirm the underlying cause of the observed diffusion changes. The term "white matter integrity" should therefore be understood with caution in the context of this study.

5.3 Areas for improvement and further work

The areas for improvement in this work are closely related to the limitations mentioned in the previous sub-point. Performing identical tests on all patients, extending the research in terms of ROI, or using more accurate diffusion MRI techniques would be strong bases for the improvement of this thesis.

Moreover, this work could be improved by developing other strategies. For example, by creating "good outcome" and "bad outcome" groups based on patients' DEWA or CAP scores, in addition to the AWRS. The AD value could also be

taken into account to broaden the scope of research.

It may also be interesting to use other MRI techniques, such as functional MRI, already used in previous studies [99, 100]. It would allow the mapping of auditory and language pathways via the identification of neuroimaging biomarkers. This would provide information on brain connectivity, and activation of auditory and linguistic pathways, and could identify potential predictors of individual cochlear implant outcomes.

Furthermore, it would be of interest to go further in the idea of prediction, via another approach than the one presented here. Indeed, the aim of this thesis is to try to predict the factors that would influence the outcome of cochlear implantation. A prediction model, as described by Z. Sun et al. in their paper "Cortical reorganization following auditory deprivation predicts cochlear implant performance in postlingually deaf adults", could therefore be a powerful tool to address this problem [60]. This would consist in trying to predict the post-CI AWRS with clinical and brain image features using machine learning and heat mapping techniques, such as random forest regression.

Chapter 6

Conclusion

Although cochlear implantation has revolutionized the treatment of post-lingual deafness in adults, it is not a miracle solution and requires a lot of expensive and exhausting steps for the patient. Therefore, predicting the outcome of cochlear implants in post-lingual deaf people remains an ongoing challenge. Moreover, the advances in medical imaging techniques, such as DTI and tractography, have opened the door to other ways of studying the brain and those regions dedicated to language and audition.

This thesis reviews theoretical concepts related to MRI and cochlear implants, as well as a review of the literature concerning the study of DTI metrics related to deafness and cochlear implants. It presents different strategies to investigate language and auditory pathways in post-lingual deaf people through tractography.

The goal of this thesis was to identify the pre-operative DTI parameters, zones and metrics, which would be linked to better recovery audition in adults suffering from post-lingual deafness. To achieve this, two strategies were used. The first consisted in dividing the patients into two groups, one considered to be "good outcome" and the other "poor outcome", and carrying out a statistical analysis to determine the significant variables between these two groups. The second consisted of a correlation analysis between post-cochlear implantation behavioral data and pre-operative MRI data. Eight white matter areas involved in auditory processing and language were investigated: the left arcuate fasciculus, the genu, body, and splenium of the corpus callosum, the left and right uncinate fasciculus, and the left and right inferior fronto-occipital fasciculus. Tractography was performed on those eight areas and four metrics were extracted for analysis: mean MD, mean FA, mean RD, and streamline count. Finally, statistical analyses were performed between those metrics and results from three 6 months post-operative audiometric tests: AWRS, DEWA, and CAP.

Results from the two strategies performed show a significantly better recovery audition (better AWRS and DEWA results) in patients with a better WM integrity (lower MD and RD values, as well as higher FA values and streamline count) in the brain areas related to audition and language (arcuate and uncinate fasciculus, corpus callosum, and IFOF) before the cochlear implantation.

These findings are consistent with previous studies, suggesting again that maintaining the microstructural integrity of these specific brain areas plays a crucial role in the success of cochlear implantation in adults with postlingual deafness. It also reinforces the idea that preoperative imaging can provide valuable information and help predict the outcome of CI.

Nevertheless, this work presents some limitations. Some behavioral data were not collected for all patients, and the AWRS tests were not carried out the same way. Moreover, other brain regions could have been investigated, such as those directly linked to audition or those with no theoretical link to audition or language. Finally, the intrinsic limitations directly linked to DTI and tractography techniques, such as crossing fiber, remain.

Despite these limitations, this thesis supports the results of previous research related to the outcome of cochlear implants in deaf people. By correlating multiple diffusion measurements with different objective auditory tests, such as AWRS and DEWA, this work sets the tone for the clinical utility of pre-operative tractography for post-lingually deaf people. It, therefore, opens new horizons in a field that is still vastly understudied and offers new prospects for improving personalized hearing care.

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Appendices

Appendix A

Behavioral data

A.1 Behavioral data pre-operative

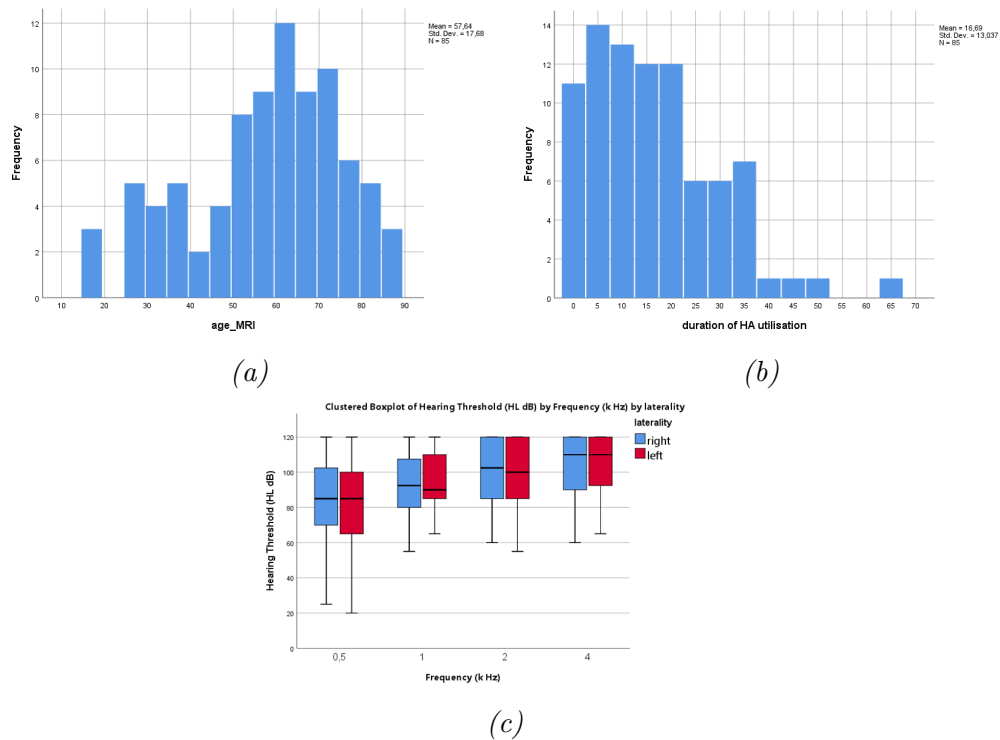


Figure A.1: Behavioral data: age of the patients (a), duration of the hearing aids before implantation (b) and pre-operative audition(c). Data collected and graph produced by Dr. Anaïs Grégoire.

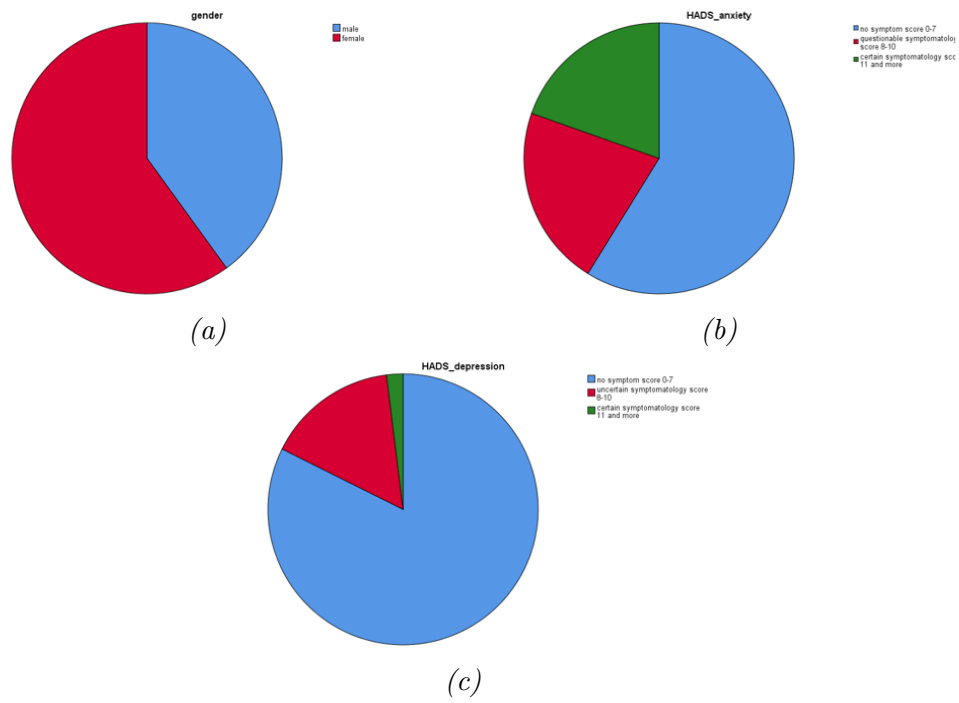


Figure A.2: Behavioral data: gender repartition(**a**), HADS anxiety (**b**) and HADS depression (**c**). Data collected and graph produced by Dr. Anaïs Grégoire.

A.2 Behavioral data - 6 months post-operative

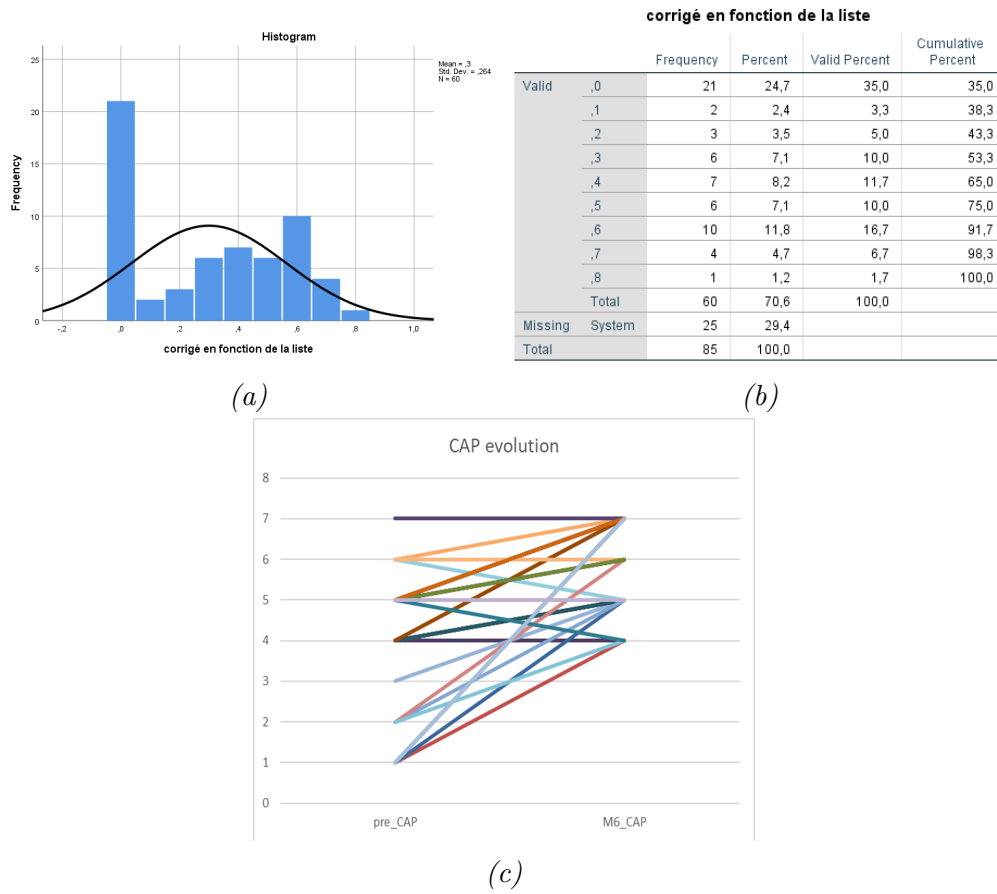


Figure A.3: Behavioral data 6 months post-operative: corrected AWRS histogram (a) and table (b) and CAP evolution (c). Data collected and graph produced by Dr. Anaïs Grégoire.

A.3 CAP scale

Category	Criteria
7	Uses telephone with known speaker
6	Understands conversation without lip-reading
5	Understands common phrases without lip-reading
4	Discriminates speech sounds without lip-reading
3	Identifies environmental sounds
2	Responds to speech sounds
1	Aware of environment sounds
0	Not aware of environmental sounds

Figure A.4: CAP scale. From [101]

Appendix B

ROI included and excluded for the eight tracked areas

Table B.1: ROIs included and excluded for the eight tracked areas, and specific threshold (default threshold = 0.5)

Areas tracked	ROIs included (AND)	ROIs excluded (NOT)
AF left	Left arcuate fasciculus(threshold = 8)	Brain stem, left putamen, left thalamus, left pallidum, left caudate, occipital lobe, right WM
CC Genu	Frontal lobe, right WM, left WM, forceps minor	Occipital lobe, temporal lobe, parietal lobe, brain stem, anterior commissure, frontal orbital cortex, medial frontal cortex
CC Body	Frontal lobe, right WM (threshold = 90), left WM (threshold = 90)	Occipital lobe, temporal lobe, parietal lobe, brain stem, forceps minor, medial frontal cortex, frontal orbital cortex
CC Splenium	Right WM (threshold = 90), left WM(threshold = 90), forceps major	Frontal lobe, brain stem, forceps minor
UF left	Uncinate Fasciculus Left (threshold = 70), left amygdala, anterior parahippocampal gyrus	Brain stem, parietal lobe, occipital lobe, insular lobe, left hippocampus, left thalamus, anterior cingulate gyrus, posterior cingulate gyrus

UF right	Uncinate Fasciculus right (threshold = 70), right amygdala, anterior parahippocampal gyrus	Brain stem, parietal lobe, occipital lobe, insular lobe, right hippocampus, right thalamus, anterior cingulate gyrus, posterior cingulate gyrus
IFOB left	IFOB left (threshold =90), left putamen, occipital lobe, frontal lobe	Brain stem, left thalamus, left pallidum, right WM
IFOB right	IFOB right (threshold =90), right putamen, occipital lobe, frontal lobe	Brain stem, right thalamus, right pallidum, left WM

Appendix C

3D registered ROIs

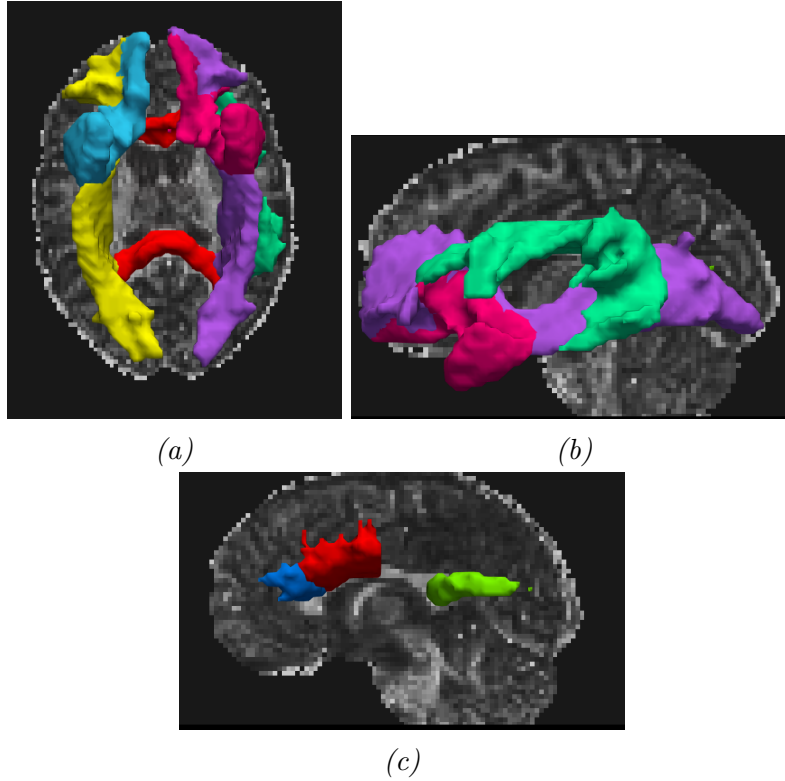


Figure C.1: 3D registered ROIs. (a) Show the eight studied areas: left AF (light green), left UF (dark pink), right UF (light blue), the Corpus callosum (red), the right IFOF (yellow), and the left IFOF (purple). (b) Zooms on the left hemisphere and shows the left AF (light green), the left UF (dark pink), and the left IFOF (purple). (c) Zooms on the CC and show the genu (dark blue), the body (red) and the splenium (green) of the CC.

Appendix D

Two sample t-test evaluation

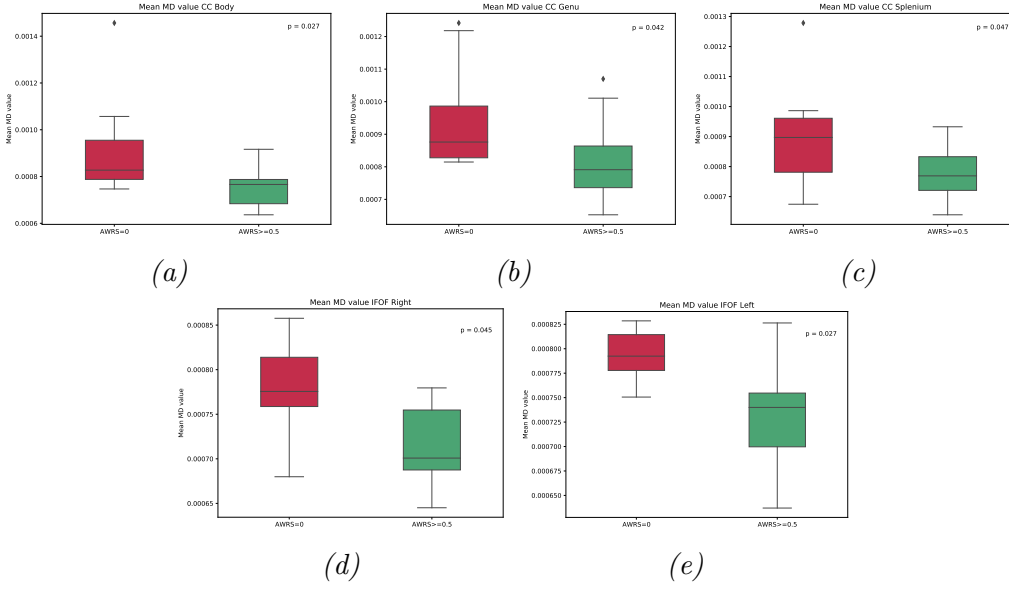


Figure D.1: Two sample t -test evaluation analysis show significantly higher values of MD in the bad-outcome group (red box-plots) compared to the good-outcome group (green box-plots) for the body of the CC (a), the genu of the CC (b), the splenium of the CC (c), the right IFOF (d) and the left IFOF (e).

Appendix E

Plots of correlation analysis

E.1 Plots of correlation analysis

E.1.1 Arcuate fasciculus

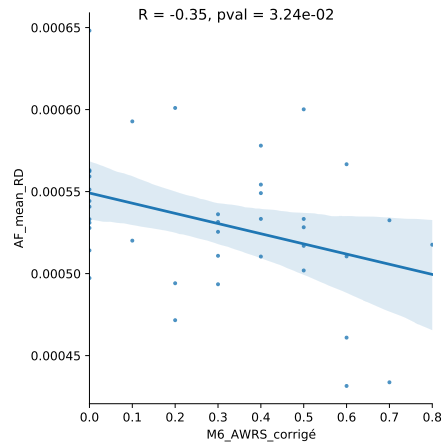


Figure E.1: AF correlation analysis between the AWRS and the mean values of RD. The line is the result of a linear regression.

E.1.2 CC Genu

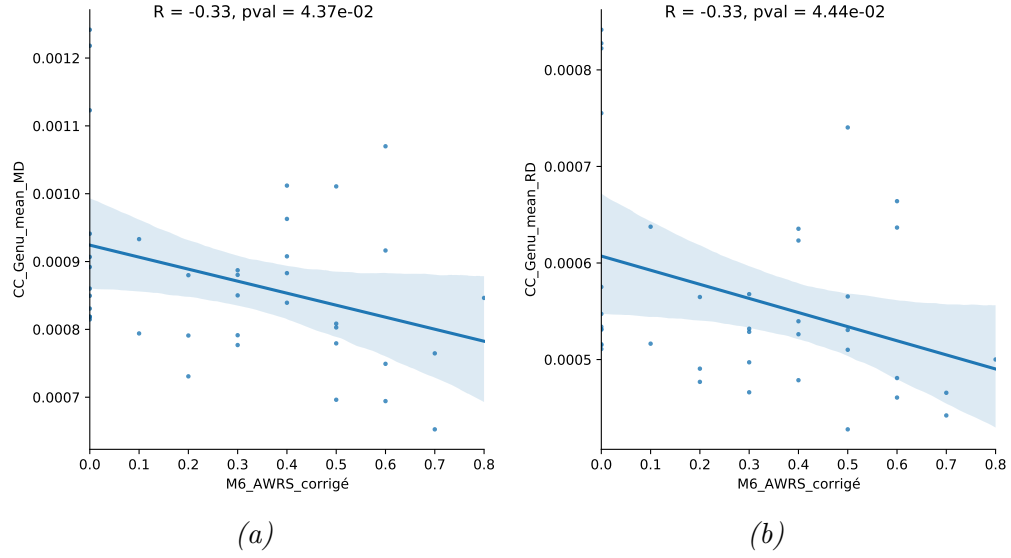


Figure E.2: The correlations between the average word recognition score (AWRS) corrected and (a) the mean MD and (b) the mean RD values of the genu of the CC. The lines are the result of a linear regression.

E.1.3 CC Body

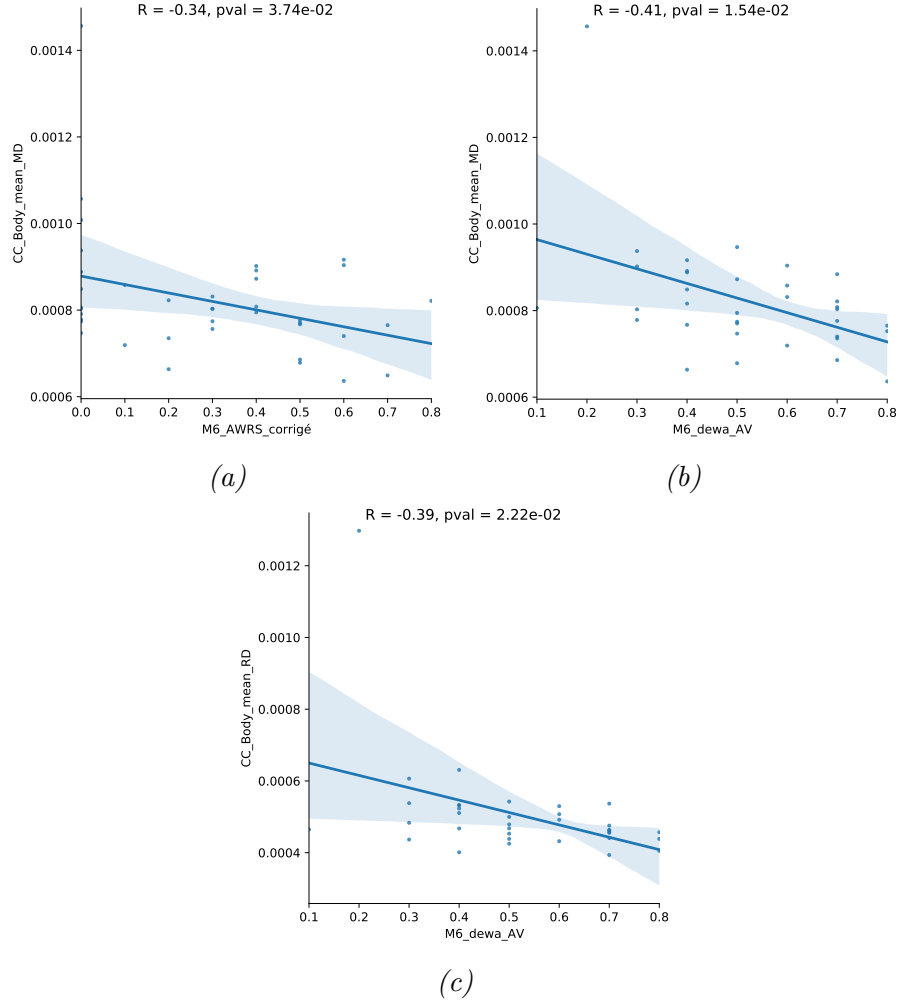


Figure E.3: CC body correlation analysis between the AWRS and mean value of MD (a) and between the DEWA and the mean values of MD (b), and RD (c). The lines are the result of a linear regression.

E.1.4 CC Splenium

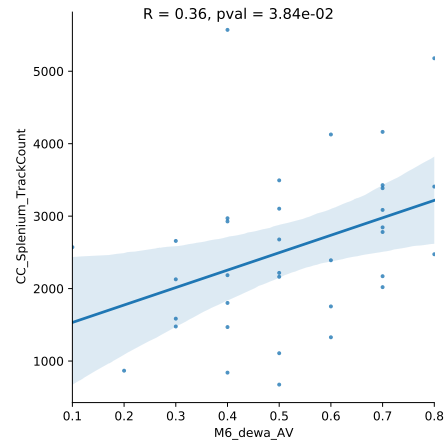


Figure E.4: CC splenium correlation analysis between the DEWA and the stream-lines count. The line is the result of a linear regression.

E.1.5 UF left

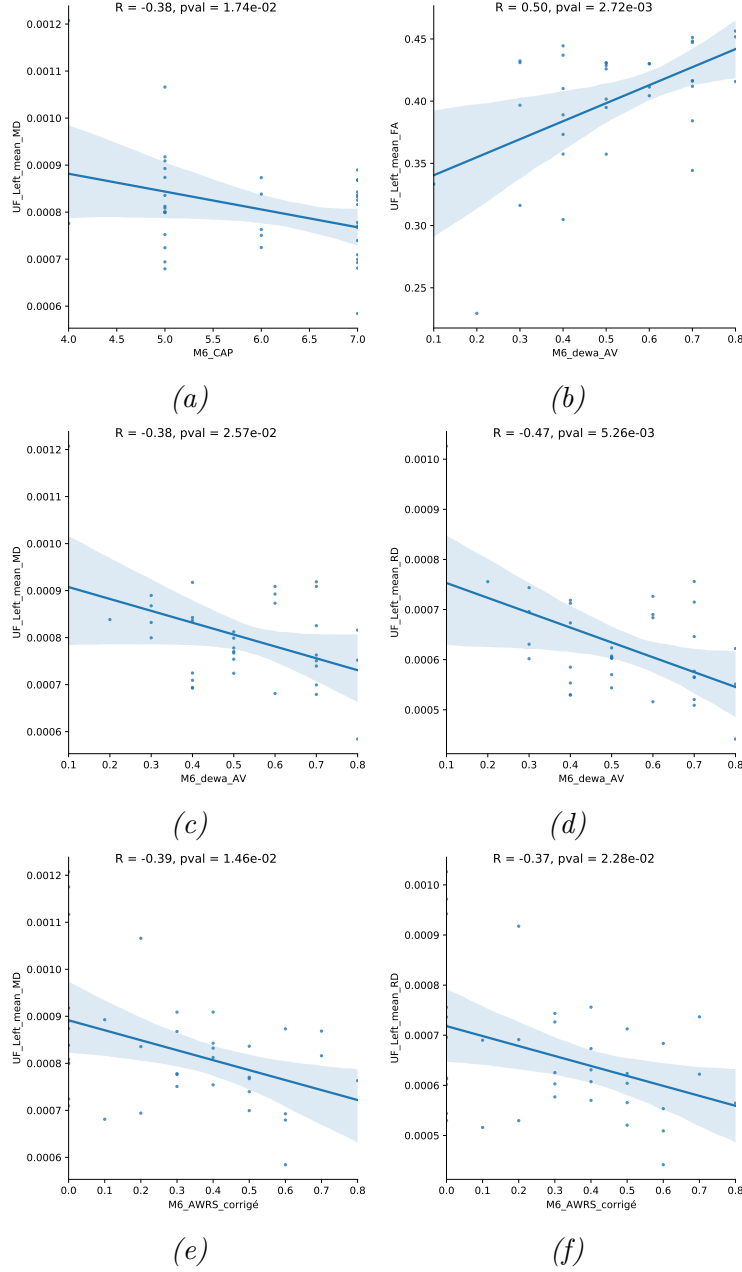


Figure E.5: Correlation between CAP score and mean MD values of the left UF (a). The correlation between the DEWA and mean value of FA (b), MD (c), and RD (d). UF left correlation analysis between the AWRS and RD mean value of MD (e), and RD (f). The lines are the result of a linear regression.

E.1.6 UF right

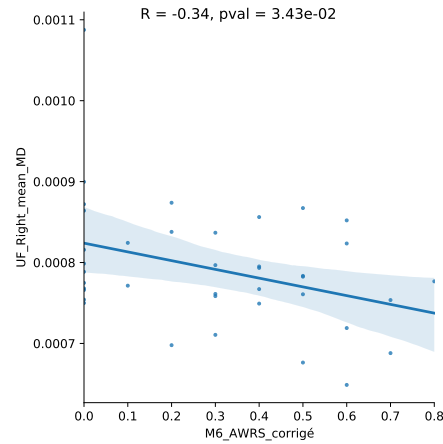


Figure E.6: UF right correlation analysis between the AWRS and the mean values of MD. The lines are the result of a linear regression.

E.1.7 IFOF right

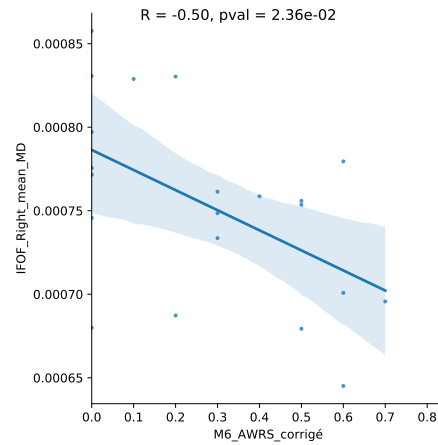


Figure E.7: IFOF right correlation analysis between the AWRS and the mean values of MD. The lines are the result of a linear regression.

E.1.8 IFOF leftt

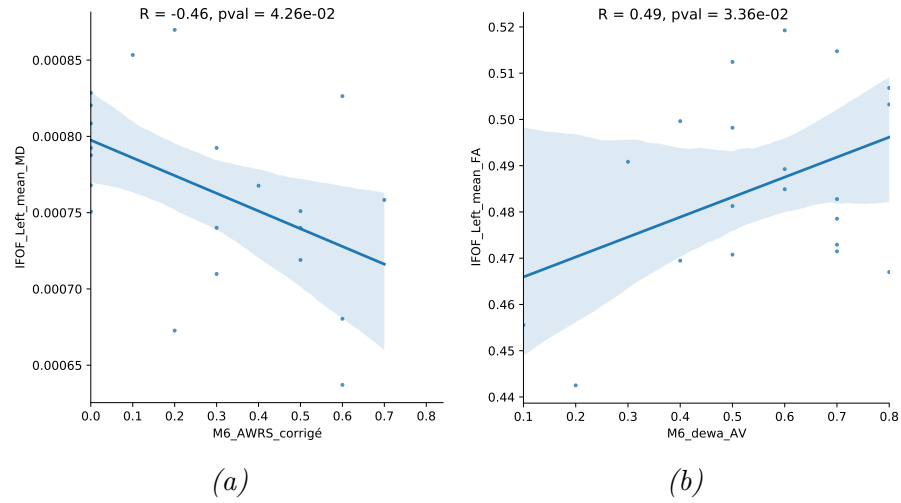


Figure E.8: IFOF left correlation analysis between the AWRS and the mean values of MD (a) and between the DEWA and the mean values of FA (b). The line is the result of a linear regression.

Appendix F

Data and results

This appendix contains the pre-operative and the 6 months post-cochlear implant behavioral data (AC score, CAP, DEWA, AWRS, etc.), as well as the data extracted from the tractography of the 8 regions of interest. The latter are presented as follows for all ROIs: mean FA, standard deviation (std) of FA, mean MD, std MD, mean RD, std RD, and track count.

Abbreviations: M6 = results 6 months post-cochlear implantation; AC = Air Conduction (performed at 0.5, 1, 2, and 4 kHz).

M6_AC_0.5	M6_AC_1	M6_AC_2	M6_AC_4	M6_AC_MEAM6_WRS_CI_M6_AWRS_C	M6_AWRS_c	M6_list	M6_CAP	M6_SIR		
40	45	50	60	48,75	0	0	0,0	2	4	5
#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
35	30	45	50	40	0,5	0,2	0,2	1	5	4
30	25	30	25	27,5	0,7	0,5	0,5	1	7	5
30	25	25	25	26,25	0,8	0,5	0,3	5	6	5
25	25	25	20	23,75	0,8	0,7	0,5	5	7	5
40	30	30	35	33,75	0,7	0,5	0,5	1	7	5
45	30	25	40	35	0,8	0,6	0,6	1	5	3
30	30	35	25	30	0,9	0,7	0,7	1	7	5
#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
30	25	35	35	31,25	0,5	0,3	0,3	1	5	5
45	40	40	40	41,25	0,7	0,5	0,3	2	4	5
40	40	55	90	56,25	0,7	0,6	0,0	2	5	5
30	30	45	50	38,75	0	0	0,0	2	5	5
25	25	20	20	22,5	0,9	0,8	#N/A	5	5	5
#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	6	5
#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
30	25	25	20	25	0,6	0,6	0,4	5	#N/A	#N/A
20	20	30	30	25	0,8	0,7	0,5	5	7	5
25	25	25	20	23,75	0,7	0,6	0,6	1	7	5
50	40	40	45	43,75	0,5	0,2	0,0	5	7	4
20	15	10	20	16,25	0,8	0,6	0,0	2	5	5
20	20	15	20	18,75	0,8	0,6	0,6	1	7	5
25	25	40	35	31,25	0,4	0,4	0,2	5	5	5
30	25	25	20	25	0,6	0,6	#N/A	5	#N/A	#N/A
40	40	40	70	47,5	0,6	0,4	0,0	2	6	5
25	20	30	25	25	0,8	0,6	0,4	5	#N/A	#N/A
30	30	35	30	31,25	0,5	0,4	0,0	2	5	5
30	30	35	30	31,25	0,9	0,6	0,6	1	6	5
50	50	40	55	48,75	0	0	#N/A	2	#N/A	#N/A
30	30	35	25	30	0,5	0,4	0,4	1	5	5

30	25	35	25	28,75	0,2	0,2	0,0	5	5	5
20	25	25	25	23,75	0,2	0,1	0,0	5	5	5
30	25	30	35	30	0,7	0,4	0,2	5	5	5
35	40	45	45	41,25	0,5	0,2	0,0	2	#N/A	#N/A
30	40	45	45	40	0,6	0,4	0,4	1	7	5
45	40	40	40	41,25	0,7	0,4	0,4	1	7	5
45	40	40	35	40	0,3	0,2	0,0	5	#N/A	#N/A
30	25	25	20	25	0,6	0,6	#N/A	5	#N/A	#N/A
40	25	35	30	32,5	0,6	0,3	#N/A	1	5	5
45	40	40	35	40	0,3	0,2	#N/A	5	#N/A	#N/A
25	25	20	25	23,75	0,9	0,8	0,8	1	6	5
45	40	40	35	40	0,3	0,2	#N/A	5	#N/A	5
30	30	35	40	33,75	0,5	0,3	0,1	5	5	5
25	25	35	20	26,25	0,8	0,6	#N/A	5	7	5
25	25	30	20	25	0,9	0,7	0,5	5	7	4
30	35	30	30	31,25	0,8	0,7	0,7	1	7	5
30	25	25	30	27,5	0,8	0,5	0,3	5	7	5
35	45	35	30	36,25	0,5	0,4	0,0	2	7	5
30	30	30	30	30	0,8	0,5	0,3	5	7	5
25	25	25	35	27,5	0,5	0,3	0,1	5	7	5

M6_dewa_A	M6_dewa_A	M6_dewa_di	AF_mean_FA	AF_stdFA	AF_mean_MI	AF_stdMD	AF_mean_RDA	AF_stdRD	AF_TrackCou	CC_Genu_me
0,1	0	0,1	0,46628321	0,09012404	0,00067157	0,00043518	0,00049728	0,00048952	39726	0,60734188
#N/A	#N/A	#N/A	0,42779359	0,11062051	0,00069206	0,00030613	0,00052903	0,00035971	32571	0,52840399
#N/A	#N/A	#N/A	0,42945016	0,09807311	0,00067523	0,00035216	0,00049411	0,00043057	23515	0,60170214
0,7	0,3	0,4	0,45750291	0,09008883	0,00071203	0,00030696	0,00052825	0,00036133	52335	0,59503326
0,7	0,3	0,4	0,48077613	0,09585536	0,00066848	0,00038102	0,00049349	0,00045849	45582	0,61145937
0,5	0,6	-0,1	0,39076563	0,10367379	0,00065418	0,00042375	0,00050191	0,00048179	20351	0,52466553
0,5	0,3	0,2	0,45985233	0,10261784	0,00072078	0,0003064	0,00053332	0,00037107	41436	0,55197411
0,7	0,5	0,2	0,48492075	0,08630604	0,00063896	0,00026478	0,00046096	0,00032846	39270	0,58024734
0,8	0,5	0,3	0,46349887	0,10790021	0,00072539	0,00021251	0,0005325	0,0002819	35230	0,60588061
#N/A	#N/A	#N/A	0,45907667	0,10632103	0,00069811	0,00047805	0,00051465	0,00056354	35066	0,54400277
0,6	0,5	0,1	0,46280767	0,10991763	0,00072765	0,0001277	0,00053617	0,00017606	33484	0,59590194
#N/A	#N/A	#N/A	0,41692233	0,08983635	0,00066291	0,0003864	0,00051085	0,00044069	39068	0,57751299
#N/A	#N/A	#N/A	0,47658251	0,10002337	0,00072879	0,00019374	0,00053101	0,00025666	44123	0,58585024
#N/A	#N/A	#N/A	0,40785941	0,08118665	0,00072013	0,00024975	0,00055923	0,0003036	42997	0,55211464
0,8	0,7	0,1	0,49032306	0,10657281	0,0007133	0,00022877	0,000512	0,00030199	36214	0,5550804
#N/A	#N/A	#N/A	0,4532555	0,11291956	0,00074257	0,00048326	0,00055614	0,00055467	38342	0,59897053
#N/A	#N/A	#N/A	0,4751832	0,09418354	0,00070021	0,00224768	0,00050993	0,00253464	32122	0,58970281
0,4	0,3	0,1	0,42987778	0,09977351	0,00070343	0,00060984	0,00053355	0,00068214	34093	0,52428453
#N/A	#N/A	#N/A	0,46137082	0,07645169	0,00069385	0,00019707	0,0005189	0,00024326	42521	0,57410538
0,7	0,6	0,1	0,47015871	0,10288375	0,00073171	0,00041297	0,00053336	0,00050123	37208	0,64595309
0,4	0,5	-0,1	0,37454404	0,0903346	0,00074865	0,00018292	0,00060016	0,00021884	34143	0,47810906
0,4	0,6	-0,2	0,43764107	0,1046099	0,0006718	0,00044665	0,0005105	0,00052738	47398	0,54631123
0,3	0,5	-0,2	0,469783	0,10301721	0,00072097	0,00031106	0,0005278	0,00037974	41937	0,55836312
0,3	0,1	0,2	0,47494591	0,12313968	0,00078186	0,00065574	0,00056305	0,0007577	35138	0,59844667
0,8	0,5	0,3	0,48399894	0,08184928	0,00059166	0,00031165	0,0004315	0,00037067	49762	0,55834412
0,4	0,3	0,1	0,47670865	0,0805716	0,00064085	0,00034822	0,00047159	0,0003922	45793	0,56804379
0,7	0,6	0,1	0,47167963	0,10938327	0,00078905	0,00077075	0,00058282	0,00083638	40401	0,59975879
0,2	0,3	-0,1	0,44628301	0,13203475	0,0007432	0,00083385	0,00053315	0,0009338	20291	0,35625256
0,5	0,5	0	0,48682582	0,0970872	0,0007059	0,00033922	0,0005104	0,00039706	53616	0,61777058
0,4	0,3	0,1	0,51139973	0,11828141	0,00078316	0,00055225	0,00054427	0,00063636	42404	0,67422626
0,6	0,5	0,1	0,4701529	0,10349535	0,00076626	0,00054541	0,00056667	0,00060291	45159	0,62695359
#N/A	#N/A	#N/A	0,49813513	0,12519135	0,00080613	0,0004841	0,00057215	0,00058958	33416	0,60943833
0,5	0,2	0,3	0,47636222	0,09387494	0,0007623	0,00023644	0,00055427	0,00030464	42920	0,64459003

#N/A	0,5	0,1	0,47633276	0,09049898	0,00074051	0,00017194	0,00054077	0,00021606	44008	0,61797592
0,5	0,3	0,2	0,46218896	0,08682831	0,00069474	0,00027295	0,00051414	0,00032613	39083	0,63154138
#N/A	#N/A	0,5	0,443901	0,10065198	0,00079617	0,00031852	0,00060099	0,00038287	35406	0,58185844
#N/A	#N/A	#N/A	0,48278788	0,1165632	0,00075752	0,00072701	0,00055124	0,00078558	37192	0,58077302
0,3	0,2	0,1	0,47221049	0,10219849	0,0007949	0,00022451	0,00057802	0,00027358	31759	0,61129645
0,4	0,5	-0,1	0,48375266	0,08434387	0,0007604	0,00041834	0,00054905	0,00048861	56468	0,56522113
#N/A	#N/A	#N/A	0,45829747	0,14605139	0,00087706	0,00108976	0,00064814	0,00116079	34749	0,5903133
#N/A	#N/A	#N/A	0,37473462	0,08898191	0,00079801	0,00100244	0,000635	0,00109336	49430	0,3345171
0,5	0,5	0	0,46896768	0,1127609	0,00080292	0,00075419	0,00058414	0,00084121	39718	0,63141404
#N/A	#N/A	#N/A	0,42555667	0,09585082	0,00082759	0,000266	0,00063508	0,00031497	33586	0,5146569
0,7	0,7	0	0,48825057	0,08558742	0,00071829	0,00022398	0,00051761	0,00029028	42568	0,62221965
#N/A	#N/A	#N/A	0,46587013	0,08804883	0,00074964	0,00026864	0,00055384	0,00032674	48919	0,64966356
0,6	0,1	0,5	0,45383981	0,11913962	0,00079929	0,00045256	0,0005928	0,00052873	37948	0,52799508
0,7	0,3	0,4	0,46573553	0,09853251	0,0007144	0,00039741	0,00052613	0,00047932	33729	0,52537876
0,7	0,7	0	0,44424567	0,08093294	0,00068603	0,00013369	0,00051693	0,00017211	36394	0,59306333
#N/A	#N/A	#N/A	0,47498769	0,10385836	0,00059301	0,00031406	0,00043373	0,00038124	45479	0,55619062
0,5	0,3	0,2	0,44450015	0,10883236	0,0007002	0,00041438	0,00052548	0,00049891	36549	0,64976614
0,4	0,2	0,2	0,46942858	0,09596525	0,00076669	0,00044895	0,00056235	0,00053883	38175	0,49599788
0,3	0	0,3	0,49693265	0,10084703	0,00074211	0,00074754	0,00053147	0,00079614	39507	0,63093863
0,6	0,3	0,3	0,46232167	0,08986579	0,00070062	0,0004998	0,00052009	0,00057058	43528	0,56366582

CC_Genu_std	CC_Genu_me	CC_Genu_std	CC_Genu_me	CC_Genu_std	CC_Genu_Tr	CC_Splenium	CC_Splenium	CC_Splenium	CC_Splenium	CC_Splenium
0,07275473	0,00083068	0,00015058	0,00053094	0,0001677	1188	0,7007536	0,06475792	0,00067451	0,00014503	0,00037066
0,06948587	0,00083053	0,00021612	0,00057974	0,00025124	256	0,65409184	0,07537497	0,00078355	0,000233	0,00047292
0,07259984	0,00079095	0,00013897	0,00049057	0,00015795	463	0,65933399	0,06782924	0,0008162	0,000146	0,00046897
0,07022362	0,00080843	0,00011513	0,00051011	0,00012961	2593	0,64409332	0,06469456	0,00081863	0,00015369	0,00049836
0,08226444	0,00085012	0,00012353	0,00052867	0,00015086	888	0,69557467	0,07111749	0,00083641	0,00019124	0,00046929
0,08853179	0,00101078	0,00025758	0,00074038	0,00028699	520	0,64900097	0,08104941	0,00079137	0,00017285	0,00047211
0,05317517	0,00080288	0,00014258	0,00053063	0,00015521	428	0,66375225	0,05548036	0,00074674	8,5232E-05	0,00041974
0,0600553	0,00074921	9,7734E-05	0,00048084	0,00010846	1008	0,66029259	0,0544899	0,00072183	0,00013173	0,00041922
0,07603646	0,00076466	8,6341E-05	0,00046558	0,00011647	2283	0,66235548	0,06425218	0,00073831	0,00014551	0,00042188
0,07843703	0,00090635	0,00023953	0,00062631	0,00025526	621	0,67372972	0,07558946	0,00073718	0,00015774	0,00041984
0,06154243	0,00088031	0,00015464	0,00056774	0,00017229	646	0,70429427	0,06150644	0,00075979	0,00010013	0,00040951
0,08008441	0,0007769	0,00013049	0,00049715	0,00015573	944	0,64388923	0,07622228	0,00074462	0,0001679	0,00044558
0,05846849	0,0008185	0,000109	0,0005159	0,00013743	395	0,67745877	0,0670454	0,00078893	9,0577E-05	0,0004362
0,05512594	0,00081472	0,00011324	0,00054724	0,0001256	2310	0,62016732	0,06777096	0,00079731	0,00014564	0,0004931
0,05059627	0,00079339	8,5455E-05	0,00052025	0,00010399	512	0,64874601	0,04797873	0,00078544	8,2923E-05	0,00044846
0,06043731	0,00084383	9,4184E-05	0,00051773	0,00011971	506	0,68442649	0,07611353	0,00089791	0,00022525	0,00052001
0,07212249	0,00087634	0,00015433	0,0005694	0,00018895	714	0,66603798	0,07148673	0,00082043	0,00016594	0,0004683
0,0849905	0,00092508	0,0003249	0,00066683	0,0003836	2253	0,58505993	0,09125058	0,00084497	0,00028298	0,00056061
0,06841143	0,00083906	0,00012099	0,00054528	0,00013621	596	0,68715743	0,06161547	0,00074131	8,5787E-05	0,00040183
0,06980638	0,00088292	0,00017229	0,00052621	0,00021078	1093	0,67103786	0,07343197	0,00071798	6,8093E-05	0,00039817
0,07427864	0,00077939	0,00012331	0,00056533	0,0001488	1345	0,59507265	0,0714869	0,00079435	0,00014842	0,00051271
0,08120059	0,0009163	0,00021374	0,0006367	0,00023264	844	0,59700579	0,0768379	0,00093261	0,00020375	0,0006046
0,05321065	0,00081869	8,6478E-05	0,000534	9,1572E-05	1637	0,66699413	0,06337074	0,00075798	7,4124E-05	0,00042034
0,08045687	0,00089201	0,00017306	0,00057521	0,00021992	2144	0,63128421	0,08756273	0,00091462	0,00028251	0,00056021
0,06054736	0,00069428	9,6229E-05	0,00046064	9,5353E-05	2615	0,63587492	0,05909962	0,0006671	0,00012833	0,00040977
0,06295706	0,00073075	0,00013042	0,00047689	0,00012566	1978	0,68382255	0,06494821	0,00071712	0,00014532	0,0004015
0,09959517	0,00097609	0,00021388	0,00062231	0,00024549	1019	0,62350578	0,11973278	0,00117479	0,00046418	0,00077369
0,09263606	0,00094105	0,00029565	0,0007552	0,00025863	8	0,71880855	0,08879263	0,00096273	0,0002217	0,00050375
0,06863973	0,00101194	0,00016392	0,00062327	0,00017743	651	0,71354025	0,06206371	0,00083072	0,00012064	0,00043098
0,08355261	0,00090683	0,00021646	0,00051497	0,00025248	3462	0,69793188	0,09681968	0,00092008	0,00023048	0,0005109
0,0683346	0,00106991	0,00019817	0,00066404	0,00021146	2425	0,69571436	0,07346312	0,00089887	0,00019007	0,0004997
0,09670221	0,00114934	0,00025156	0,00074303	0,00031848	1829	0,66670776	0,08789622	0,0010633	0,0002231	0,0006259
0,07092525	0,00083926	0,00012215	0,0004786	0,00014848	1299	0,6906016	0,07988919	0,00091008	0,00021913	0,00050996

0,05948582	0,00084957	0,0001294	0,0005109	0,00015433	618	0,71190033	0,07091728	0,00087955	0,00019476	0,00046829
0,07221054	0,0008601	0,0001986	0,00053164	0,00023818	816	0,69580005	0,06661992	0,00074871	0,00011966	0,00041059
0,06456553	0,00087986	0,00013043	0,00056477	0,00014083	1154	0,69402766	0,06467399	0,00083289	0,00014825	0,00045734
0,07667613	0,00121811	0,00025842	0,00082232	0,00028442	337	0,64859883	0,08790967	0,00098629	0,0001865	0,0005858
0,04213168	0,00090769	4,9967E-05	0,00053965	6,6521E-05	640	0,66811919	0,05268049	0,00089941	0,00013057	0,00050202
0,07280963	0,00096285	0,00019825	0,00063546	0,00022052	222	0,68869442	0,07448217	0,00095644	0,00019891	0,00054498
0,09037611	0,00124171	0,00030799	0,00082754	0,00036124	1890	0,59227357	0,15207973	0,00127848	0,00049646	0,00087244
0,06187849	0,00111471	0,00026068	0,00092877	0,00024631	1002	0,62828821	0,09244308	0,00086457	0,00022127	0,0005303
0,08499137	0,00097165	0,00019587	0,00059132	0,00022181	711	0,75059743	0,07051971	0,00087676	0,00017169	0,00044065
0,0613157	0,00090028	0,00014639	0,00062601	0,00015824	573	0,70646271	0,07334177	0,00091079	0,00022635	0,00049611
0,06530493	0,00084637	9,2126E-05	0,00050006	0,00011374	1850	0,69789348	0,07109893	0,00087568	0,00019861	0,00047345
0,05276652	0,00082401	6,1886E-05	0,000461	7,6754E-05	894	0,69300536	0,06316423	0,00084843	0,00011248	0,00045284
0,07120505	0,00093303	0,0001198	0,00063759	0,00014695	146	0,69348187	0,0630362	0,00087386	0,00013035	0,0004831
0,07560945	0,00105747	0,00030481	0,00077101	0,00032765	592	0,67706872	0,0698128	0,0008006	0,00018392	0,00045823
0,06538664	0,00069625	5,5563E-05	0,0004277	8,5033E-05	1528	0,702196	0,05345929	0,00071746	0,00011058	0,00038846
0,07548151	0,00065262	0,00014659	0,0004421	0,00016526	1040	0,68933952	0,07140894	0,00063937	0,0001548	0,0003576
0,07249012	0,00079138	0,00012239	0,00046609	0,00015322	1801	0,67828639	0,08052981	0,00072844	0,0001183	0,00040798
0,10904496	0,00112297	0,00029117	0,00084159	0,00033867	1082	0,6759542	0,08617887	0,0009604	0,00028508	0,00054926
0,07146549	0,00088719	0,00017152	0,00053191	0,00017844	1503	0,73378437	0,06048109	0,00085416	0,00013566	0,00042845
0,05986436	0,00079402	0,0001137	0,00051644	0,00012329	1523	0,70649472	0,0710076	0,00073963	0,0001109	0,0003922

CC_Splenium	CC_Splenium	CC_Body_me	CC_Body_std	CC_Body_me	CC_Body_std	CC_Body_me	CC_Body_std	CC_Body_Tra	UF_Left_me	UF_Left_std
0,00016484	2572	0,65992929	0,05904038	0,00080604	0,00012738	0,00046467	0,00013951	1359	0,33337701	0,07704023
0,00029331	381	0,56854638	0,06512172	0,00073866	9,0734E-05	0,0004765	0,00011286	518	0,38710446	0,07495936
0,00015502	3567	0,493489	0,1205657	0,00073509	0,00025706	0,0004573	0,00025237	601	0,33232733	0,08225387
0,00016668	3428	0,62938877	0,0599931	0,00077614	8,2954E-05	0,00045776	9,158E-05	2417	0,45119102	0,06569986
0,00021372	3386	0,63211156	0,06612267	0,00080316	0,00011024	0,00047555	0,00012524	1247	0,41647831	0,07972239
0,00019398	2163	0,3841781	0,13139357	0,00067844	0,00032258	0,00046777	0,00031002	272	0,35741148	0,05304356
8,5437E-05	3103	0,58679253	0,05008606	0,00077036	5,8896E-05	0,00047873	7,2273E-05	186	0,39488913	0,06259292
0,00013974	4163	0,62069432	0,04947797	0,00074008	6,941E-05	0,00044071	7,5747E-05	612	0,44829622	0,05901211
0,00016657	5179	0,6453973	0,05030969	0,00076518	0,00010045	0,00043844	0,00011295	2434	0,41578132	0,06154882
0,00017222	2506	0,61609002	0,05915654	0,00082978	0,00014058	0,00051033	0,00015055	739	0,32039337	0,06291219
0,00011667	1328	0,6227393	0,06051013	0,00083135	0,00014484	0,00050729	0,00015214	1241	0,40436338	0,06344814
0,0001671	3084	0,55766601	0,07222855	0,00075642	9,8532E-05	0,00049376	0,0001049	1403	0,36242089	0,06426154
0,00010673	2488	0,61587782	0,04846242	0,00077383	6,7168E-05	0,00045914	7,7167E-05	562	0,41770997	0,06038274
0,00014432	4152	0,5706623	0,05113021	0,00079093	0,00010785	0,00050848	0,00011287	3243	0,31471053	0,0520471
8,3143E-05	2474	0,59822812	0,03871353	0,00075252	3,521E-05	0,00045705	4,6837E-05	589	0,45634384	0,04980909
0,00026884	1015	0,60898609	0,04570598	0,00077278	5,9243E-05	0,00046274	6,5787E-05	1908	0,38750336	0,06952991
0,00016579	2667	0,60876936	0,05753164	0,00078817	9,4026E-05	0,00047636	0,00010694	933	0,40350411	0,04845796
0,00031129	2185	0,57588955	0,05513693	0,00081614	0,0001178	0,0005233	0,00013118	1485	0,35748295	0,04523319
0,00010394	2108	0,6171502	0,05281163	0,00082659	0,00010515	0,00049435	0,00010162	1635	0,44187268	0,06730365
8,6167E-05	2781	0,65102853	0,06996952	0,00080791	0,00017645	0,00046324	0,0002115	1778	0,34423216	0,09161697
0,00015894	5571	0,51310153	0,05675864	0,00076717	6,4715E-05	0,0005319	8,194E-05	1746	0,3048146	0,04883413
0,00019633	840	0,54152229	0,06420899	0,00091647	0,00021952	0,00063071	0,00021769	851	0,38895669	0,08698997
8,6015E-05	1585	0,59084519	0,04910721	0,00077836	7,9442E-05	0,0004834	8,9788E-05	648	0,39674223	0,05286746
0,00033894	1477	0,58602222	0,05837323	0,0009375	0,0001493	0,00060653	0,00015712	429	0,43098162	0,05501372
0,00013029	3408	0,57963304	0,05441248	0,00063646	9,6465E-05	0,00040514	9,3422E-05	5256	0,45166083	0,07040137
0,00014467	2971	0,61431222	0,05554485	0,00066352	7,2742E-05	0,00040101	7,4755E-05	1452	0,43695043	0,0753697
0,00056266	2020	0,60814068	0,08087822	0,00088411	0,00027307	0,00053678	0,00032427	557	0,41193085	0,07970397
0,00026267	867	0,23299477	0,00326987	0,00145648	7,0331E-06	0,00129761	7,781E-06	1	0,22944232	0,00046341
0,00012786	1108	0,63760939	0,05652912	0,00087237	0,00013914	0,0004998	0,00012615	542	0,42590818	0,0606582
0,00030818	1802	0,69442168	0,06469716	0,00088823	0,00016839	0,0004674	0,00020319	1966	0,41013052	0,08383083
0,00021962	2391	0,63043522	0,05797962	0,00090382	0,00016661	0,00052966	0,00016515	1143	0,41136194	0,07022551
0,00025764	1455	0,62828878	0,07942199	0,00106326	0,00018039	0,00064148	0,00021749	1568	0,38073016	0,07086143
0,00024217	3494	0,65203316	0,06206092	0,00079464	8,4673E-05	0,00043848	9,456E-05	1849	0,4304648	0,04684091

0,00022034	3093	0,65105825	0,06224694	0,00080302	9,7262E-05	0,00044191	0,00010609	1438	0,41710813	0,07083586
0,00012014	2678	0,64658652	0,05615906	0,00074688	0,00011177	0,00042504	0,00011688	2382	0,43094014	0,06751904
0,00016998	2390	0,64560093	0,06386882	0,00082268	0,00010711	0,00046598	0,00011198	1797	0,28706485	0,07448219
0,00022189	402	0,61287313	0,06633796	0,00105696	0,00019726	0,00066161	0,0002138	796	0,3617823	0,11612463
0,00013722	2128	0,60876557	0,03962197	0,00090187	5,0263E-05	0,00053812	6,1955E-05	402	0,4323105	0,05370264
0,00021242	1469	0,61799881	0,06043287	0,0008915	0,00016215	0,00053275	0,0001744	553	0,3732821	0,07483704
0,00061747	3745	0,61836341	0,06669999	0,00100804	0,00018557	0,00061189	0,00020085	1798	0,33411313	0,10128079
0,00025686	4728	0,42456226	0,06383452	0,0008786	0,00464504	0,00067106	0,00520944	1196	0,33580894	0,10044956
0,00019463	675	0,65768169	0,06742946	0,00094663	0,00015536	0,0005424	0,00017821	1088	0,42867261	0,06041096
0,00025525	2291	0,59882994	0,05006586	0,00082709	5,2934E-05	0,00049748	7,062E-05	705	0,31753701	0,05476035
0,00021816	3086	0,64281557	0,05294078	0,00082129	7,8777E-05	0,00046243	9,2323E-05	1700	0,44718533	0,05581268
0,00011511	1564	0,63186256	0,04047914	0,00079751	5,4382E-05	0,00045581	6,3473E-05	628	0,39189575	0,05223808
0,00015094	1754	0,63685286	0,05677647	0,00085787	9,9045E-05	0,00049157	0,00012577	693	0,43016635	0,08607359
0,00019285	2171	0,59343307	0,05383647	0,00073562	7,0142E-05	0,00045539	8,2081E-05	503	0,38417259	0,0909406
0,0001116	2845	0,63768864	0,05323835	0,00068571	4,8129E-05	0,00039345	6,4018E-05	2300	0,41611652	0,07519286
0,00016333	4559	0,64263592	0,0545543	0,0006492	0,00010374	0,00038169	0,00011453	2771	0,35628665	0,09783931
0,00012779	2217	0,63405974	0,0657187	0,00077422	9,7312E-05	0,00045303	0,00011325	1738	0,40165999	0,04955168
0,00033362	2927	0,61022871	0,06395097	0,0008487	0,00013143	0,00051059	0,00014662	3172	0,44443042	0,06511348
0,00013933	2658	0,65927151	0,05805752	0,00080291	9,2961E-05	0,00043651	0,00010106	1362	0,3162497	0,05794075
0,00012734	4127	0,60833089	0,05307857	0,00071916	5,8321E-05	0,00043201	7,1738E-05	1689	0,43000711	0,06945816

UF_Left_mea	UF_Left_std	UF_Left_mea	UF_Left_std	UF_Left_Trac	UF_Right_me	UF_Right_std	UF_Right_me	UF_Right_std	UF_Right_me	UF_Right_std
0,00120733	0,00081548	0,00102607	0,00080849	60	0,41847233	0,06779323	0,00075413	0,00062507	0,00059163	0,00065363
0,00080911	0,00079503	0,00064716	0,00081246	69	0,41580582	0,06596838	0,00073887	0,00037972	0,00056876	0,00040831
0,00083554	0,00021067	0,00069124	0,00023069	31	0,36386703	0,06481622	0,00083789	0,00025386	0,00067779	0,00026621
0,00069935	8,1233E-05	0,00052065	9,6605E-05	83	0,38190387	0,05408802	0,00076075	0,00014818	0,00060276	0,00016006
0,00075066	0,00060029	0,00057692	0,00059461	67	0,38260122	0,0812908	0,00079677	0,00029865	0,00063053	0,00032146
0,00077041	0,00049139	0,00062353	0,0005045	55	0,35844242	0,06618649	0,00078249	0,0003453	0,00063203	0,00035265
0,00076726	0,00047554	0,00060418	0,0004672	60	0,39261902	0,0675436	0,00086729	0,00061911	0,00068722	0,0005679
0,00067927	0,00030553	0,00050909	0,00032292	59	0,44149779	0,04419279	0,00071903	4,5507E-05	0,00053675	5E-05
0,00081602	0,00031833	0,00062236	0,00031755	26	0,43604653	0,05256029	0,00068805	4,5109E-05	0,00051403	5,4032E-05
0,00079997	6,9379E-05	0,00066244	9,5302E-05	12	0,3693138	0,05697324	0,00075783	0,00017514	0,0006056	0,00015366
0,00090889	0,00035143	0,00072649	0,00036083	34	0,38182481	0,0699423	0,00083682	0,00046641	0,00066829	0,00043449
0,00077606	0,00032302	0,00062545	0,0003155	53	0,37098324	0,0667544	0,00075851	0,0001652	0,00060532	0,00017871
0,00080847	0,00035059	0,00061466	0,00034081	24	0,44127863	0,05789205	0,00078855	0,00024875	0,00058897	0,00025275
0,00087383	0,00058738	0,00073626	0,00055108	110	0,31509652	0,05272841	0,00087207	0,00054027	0,00072948	0,00051448
0,00075208	4,4324E-05	0,00055125	4,9082E-05	39	0,39235505	0,09511941	0,00091748	0,00043624	0,00073423	0,00048593
0,0007596	0,00038221	0,00060325	0,00038109	7	0,44497915	0,05208008	0,0007647	4,3509E-05	0,00056864	6,0572E-05
0,00073207	5,4131E-05	0,00056204	5,1846E-05	25	0,44310177	0,06232919	0,00075439	4,0236E-05	0,00056555	5,5758E-05
0,00072471	4,8717E-05	0,0005851	5,0851E-05	71	0,36188174	0,0644983	0,00079308	0,00048423	0,00064107	0,00051213
0,00072526	0,00010091	0,00054605	0,0001234	134	0,46887667	0,07435794	0,00072912	6,0349E-05	0,00053208	8,8813E-05
0,00090902	0,00039654	0,00075605	0,00039255	35	0,36580991	0,08115356	0,00079333	0,00033222	0,00063791	0,00035076
0,0008364	0,00036999	0,0007126	0,00036856	181	0,36147429	0,05037311	0,00078352	0,00015968	0,00063938	0,00016597
0,00069259	0,00010806	0,00055348	0,00012596	51	0,33394559	0,06905075	0,00085209	0,00040855	0,00069896	0,00044066
0,00088973	0,00057081	0,00069581	0,00055607	48	0,41929946	0,04121187	0,00076799	4,3293E-05	0,00058374	4,6007E-05
0,00079962	5,1934E-05	0,00060191	6,9086E-05	37	0,41486401	0,08001786	0,00077483	0,00019469	0,00060001	0,00020661
0,00058429	7,6132E-05	0,00044165	9,3144E-05	126	0,46875221	0,06093224	0,00064876	6,2714E-05	0,00047738	7,6937E-05
0,00069407	0,00034279	0,00052956	0,00038313	122	0,42074048	0,05931268	0,00069787	0,00010734	0,00053226	0,00012466
0,00091868	0,00072583	0,00071489	0,00075106	55	0,44877189	0,08044125	0,00088513	0,00054776	0,00066476	0,00057541
0,0008384	1,6897E-05	0,00075565	1,5325E-05	1	0,40217227	0,06416333	0,00089971	0,00023978	0,0007015	0,00022546
0,00075411	9,0199E-05	0,00057012	0,00010614	107	0,42561586	0,08458452	0,00074924	0,00054742	0,00056961	0,00057918
0,00091746	0,00073577	0,00071858	0,00073588	28	0,44980054	0,07970845	0,00079867	0,00048493	0,00059225	0,00049963
0,00087326	0,00066565	0,00068372	0,00068697	163	0,42582746	0,07448072	0,00082353	0,00040392	0,00062466	0,00042734
0,00089503	0,00031726	0,00071909	0,00033205	23	0,40327497	0,06707683	0,00087901	0,00010392	0,00067565	0,00012728
0,00081234	3,3574E-05	0,00060722	4,2687E-05	61	0,43982969	0,06832903	0,00076715	0,00029085	0,00057027	0,00029731

0,00080071	0,00014501	0,00061305	0,00018144	50	0,43567513	0,06082344	0,00081577	0,00041402	0,0006127	0,00037781
0,00072413	8,1655E-05	0,00054383	0,00011105	27	0,39102888	0,07473282	0,00074996	9,0046E-05	0,0005861	0,00011123
0,00106599	0,00056444	0,00091753	0,00054283	97	0,35079472	0,08825298	0,00087387	0,0002037	0,00070816	0,00021641
0,00111684	0,00066855	0,00094229	0,00069656	34	0,39314268	0,09391102	0,00108751	0,00043027	0,00087794	0,00045516
0,00083223	5,1534E-05	0,00063088	5,4839E-05	18	0,43372324	0,0487217	0,00085617	0,00019314	0,000641	0,00019665
0,00084278	0,00066335	0,00067338	0,00065254	139	0,39969984	0,07352452	0,00079513	0,00010107	0,00062083	0,00010937
0,00117518	0,00015366	0,00097151	0,00018076	8	0,42570821	0,08831997	0,00086411	0,0003966	0,00066953	0,00043602
0,00107212	0,00034487	0,00089482	0,00030852	47	0,39066619	0,10294262	0,00095825	0,00077182	0,00078887	0,0007763
0,00079893	5,3319E-05	0,00060323	5,0733E-05	46	0,37988772	0,10255414	0,00091499	0,00027512	0,00073385	0,00031697
0,00093398	0,00021723	0,00077919	0,00022381	88	0,40402942	0,07853307	0,00093702	0,0004509	0,00074712	0,00047875
0,00076299	0,00013732	0,00056447	0,00014817	156	0,45480463	0,05973467	0,00077675	0,00029131	0,00057165	0,0003327
0,00079031	0,00024128	0,00061596	0,00027709	40	0,46540075	0,08573322	0,00075997	5,8239E-05	0,00054849	8,017E-05
0,00089268	0,00047167	0,00069006	0,00049845	128	0,3937328	0,08071842	0,0008243	0,00018726	0,00064396	0,00020814
0,00082535	0,00020245	0,00064601	0,000231	5	0,41395533	0,07281604	0,00075581	0,00024153	0,00057695	0,00024131
0,00073954	0,00031434	0,00056558	0,00032092	77	0,43755283	0,06777912	0,00067639	0,00018753	0,00050984	0,00021022
0,0008685	0,00068848	0,00073667	0,00065489	31	0,36628585	0,05442996	0,00075361	0,00029902	0,00063158	0,00029775
0,00077802	5,8842E-05	0,00060288	6,8148E-05	65	0,45510082	0,06036513	0,00076117	0,00030024	0,00056195	0,00032622
0,00070931	0,00010743	0,00052987	0,00011142	69	0,41676536	0,05561646	0,00076602	0,0002936	0,00058708	0,0003043
0,00086763	0,00060047	0,00074359	0,00058525	167	0,37113048	0,06888884	0,00071062	0,00019497	0,00057702	0,00020092
0,00068108	5,0126E-05	0,00051598	6,6754E-05	173	0,44762212	0,06280504	0,0007714	7,2736E-05	0,00057156	9,3669E-05

UF_Right_Tr	IFO_Left_m	IFO_Left_st	IFO_Left_m	IFO_Left_st	IFO_Left_m	IFO_Left_st	IFO_Left_Tr	IFO_Right_n	IFO_Right_s	IFO_Right_n
81	0,45556313	0,02440556	0,00078765	9,8582E-05	0,00059084	9,5123E-05	18	0,49339131	0,03400262	0,00067991
131	0,46555526	0,03528959	0,00079733	0,00011887	0,00058837	0,00012573	37	0,47615481	0,0327684	0,00075274
109	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
178	0,47148274	0,0258849	0,00075099	3,2533E-05	0,00054438	2,9949E-05	90	0,462896	0,03062957	0,00075591
57	0,48278374	0,02417767	0,00074007	3,627E-05	0,00053269	3,507E-05	16	0,4646881	0,03324382	0,00076136
50	0,47076943	0,03070985	0,00074	3,4715E-05	0,00053543	4,1269E-05	67	0,45840354	0,02909246	0,00075357
25	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
29	0,47852844	0,03230023	0,00068042	2,775E-05	0,00049126	2,948E-05	103	0,46963242	0,02527423	0,00070082
100	0,46700158	0,02668186	0,00075832	2,497E-05	0,00054981	2,8775E-05	49	0,49266316	0,03030859	0,00069568
64	0,47699453	0,0308233	0,00074328	3,9692E-05	0,00053158	4,0802E-05	71	0,50619135	0,04094555	0,00068323
52	0,48490844	0,02084794	0,00079244	5,0746E-05	0,00056397	4,6743E-05	6	0,46307018	0,03531173	0,00074847
160	0,43881587	0,030685	0,00070979	4,7514E-05	0,00052985	5,0841E-05	110	0,43530632	0,04003115	0,0007336
74	0,50877877	0,02778289	0,00076797	2,0396E-05	0,00052979	2,4516E-05	68	0,50316202	0,02752202	0,00077559
135	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
22	0,50323915	0,03453567	0,00075242	2,3971E-05	0,00052382	3,2981E-05	45	0,52062269	0,02834504	0,00077396
40	0,48760313	0,01641943	0,00082627	3,4979E-05	0,00058643	2,9192E-05	6	0,48970447	0,02659321	0,00079607
92	0,49128222	0,02460524	0,00075025	4,1739E-05	0,00052882	4,1298E-05	14	0,49914449	0,03396882	0,0007656
77	0,4694709	0,03320868	0,00074396	3,0757E-05	0,00053905	3,0152E-05	59	0,45815208	0,03904993	0,00074959
109	0,48257704	0,03184071	0,00074461	3,6502E-05	0,00053474	3,7E-05	133	0,51185606	0,02558413	0,00074653
77	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
344	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
42	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
96	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
114	0,49084482	0,02892238	0,0008085	2,6323E-05	0,0005717	3,2583E-05	34	0,51320212	0,03064223	0,00077157
117	0,50680557	0,03457132	0,00063708	3,578E-05	0,00044504	3,4067E-05	637	0,51684703	0,03049251	0,00064511
124	0,499631	0,03532376	0,0006727	3,6543E-05	0,0004734	4,0787E-05	420	0,49590791	0,03282229	0,00068726
55	0,51474677	0,04016605	0,00084249	5,6234E-05	0,00058511	5,9015E-05	29	0,52145976	0,03687608	0,00081616
32	0,44250706	0,03096096	0,0008285	1,3519E-05	0,00060805	1,2585E-05	4	0,5054176	0,03329644	0,00083062
151	0,51243527	0,03212438	0,00076765	4,3294E-05	0,00052919	4,2203E-05	321	0,53082967	0,03300593	0,00075864
107	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
132	0,51925676	0,03705565	0,00082636	9,2216E-05	0,0005758	9,192E-05	82	0,5116197	0,03009738	0,00077954
37	0,47124189	0,03834385	0,00081531	5,415E-05	0,00060035	5,6633E-05	14	0,48879468	0,0539246	0,0008634
186	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A

70	0,5365497	0,03963608	0,00082036	0,00010155	0,0005508	0,00011046	219	0,52158332	0,03450722	0,00079716
42	0,48127002	0,02459946	0,00075058	2,2513E-05	0,00053382	2,1378E-05	65	0,46962618	0,03430925	0,00074573
66	0,44881261	0,04057601	0,00086982	0,00016391	0,00065065	0,00017115	26	0,48862926	0,03806537	0,00083031
32	0,5138115	0,03054949	0,00079243	2,4446E-05	0,00054948	1,9766E-05	6	0,48209615	0,02564167	0,00085763
39	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
266	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
92	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
56	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
82	0,49819793	0,04099937	0,00084775	4,3758E-05	0,00059196	4,4331E-05	93	0,47764005	0,03985707	0,00085913
23	0,48150807	0,04032577	0,00084192	3,8772E-05	0,00060002	4,5332E-05	93	0,55176628	0,03497877	0,00084315
150	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
77	0,51536859	0,03623514	0,00079559	3,5133E-05	0,00054481	3,8657E-05	134	0,53201877	0,03472295	0,00079835
173	0,48926227	0,03376657	0,00085335	4,0714E-05	0,00060253	4,6941E-05	71	0,47761476	0,02279356	0,00082884
21	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
122	0,47291747	0,02365538	0,00071899	3,0582E-05	0,00051963	3,0098E-05	56	0,50010556	0,0296024	0,00067933
30	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
93	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
62	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
147	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
127	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A

IFOF_Right_s	IFOF_Right_n	IFOF_Right_s	IFOF_Right_T	age_MRI	duration_HA	pre_R_AC_0	pre_R_AC_1	pre_R_AC_2	pre_R_AC_4	pre_R_AC_m
5,0842E-05	0,00048721	5,6099E-05	45	73	11	120	120	120	115	118,75
7,5108E-05	0,00054724	8,5576E-05	55	71	35	80	85	120	120	101,25
#N/A	#N/A	#N/A	#N/A	43	0	75	85	100	120	95
3,8192E-05	0,00055312	3,9209E-05	215	65	10	65	65	70	80	70
4,5428E-05	0,00055288	4,3601E-05	60	77	35	110	100	100	110	105
2,544E-05	0,00055361	2,9352E-05	63	68	25	45	100	120	120	96,25
#N/A	#N/A	#N/A	#N/A	50	10	85	100	120	120	106,25
2,8427E-05	0,00051257	2,7187E-05	120	41	3	80	75	75	75	76,25
2,5333E-05	0,00049111	2,8301E-05	291	27	12	65	90	110	100	91,25
3,3076E-05	0,00047802	4,0383E-05	397	50	15	50	85	115	120	92,5
3,5249E-05	0,00054421	4,2401E-05	171	60	2	90	115	120	120	111,25
7,6567E-05	0,0005559	7,8509E-05	233	37	3	120	120	120	120	120
3,0936E-05	0,0005415	3,1211E-05	27	17	6	25	85	120	120	87,5
#N/A	#N/A	#N/A	#N/A	53	11	70	90	95	75	82,5
2,2852E-05	0,00052765	2,7179E-05	71	30	2	80	100	120	120	105
2,5745E-05	0,00056336	2,3952E-05	31	53	4	50	65	80	90	71,25
4,7174E-05	0,00054248	4,846E-05	27	47	36	95	95	85	105	95
3,7003E-05	0,00055444	4,2612E-05	141	75	11	80	85	75	75	78,75
3,216E-05	0,00051821	3,1766E-05	39	64	36	100	105	120	120	111,25
#N/A	#N/A	#N/A	#N/A	61	12	85	80	90	95	87,5
#N/A	#N/A	#N/A	#N/A	68	17	90	95	95	100	95
#N/A	#N/A	#N/A	#N/A	26	1	105	100	105	110	105
#N/A	#N/A	#N/A	#N/A	27	22	115	115	120	120	117,5
3,8592E-05	0,0005369	3,6585E-05	146	74	15	85	85	95	110	93,75
2,6678E-05	0,00044828	2,726E-05	117	50	23	120	120	120	120	120
3,8759E-05	0,00048671	4,0333E-05	418	62	0	45	90	120	120	93,75
5,2668E-05	0,00055933	5,7861E-05	90	81	35	120	120	120	120	120
5,4022E-05	0,00057646	5,3282E-05	19	81	14	50	55	75	90	67,5
5,4301E-05	0,0005125	5,9285E-05	88	61	12	60	65	75	90	72,5
#N/A	#N/A	#N/A	#N/A	68	63	70	80	85	110	86,25
5,8599E-05	0,00054134	6,0595E-05	30	85	8	80	75	80	100	83,75
5,1911E-05	0,00061972	7,6327E-05	8	88	20	105	90	95	110	100
#N/A	#N/A	#N/A	#N/A	69	12	120	120	120	120	120

3,5715E-05	0,00054297	3,916E-05	56	34	31	100	105	100	80	96,25
3,5237E-05	0,0005433	3,8018E-05	62	63	15	55	70	75	75	68,75
6,6995E-05	0,00059255	6,6238E-05	40	71	3	75	70	65	75	71,25
3,1022E-05	0,00061443	3,9464E-05	6	86	25	90	120	120	120	112,5
#N/A	#N/A	#N/A	#N/A	72	2	80	75	90	115	90
#N/A	#N/A	#N/A	#N/A	60	17	85	95	90	95	91,25
#N/A	#N/A	#N/A	#N/A	80	5	60	75	80	90	76,25
#N/A	#N/A	#N/A	#N/A	82	15	60	65	85	120	82,5
3,9145E-05	0,00061429	4,507E-05	8	75	22	85	90	85	75	83,75
5,016E-05	0,00055526	4,512E-05	21	73	0	70	115	115	120	105
#N/A	#N/A	#N/A	#N/A	60	10	100	100	120	120	110
3,7128E-05	0,00054012	4,3448E-05	302	59	11	90	95	90	110	96,25
4,5424E-05	0,00059168	3,2308E-05	18	72	37	90	95	85	90	90
#N/A	#N/A	#N/A	#N/A	79	30	105	120	120	120	116,25
5,1945E-05	0,0004822	4,7408E-05	122	69	30	80	95	120	120	103,75
#N/A	#N/A	#N/A	#N/A	59	51	60	75	115	110	90
#N/A	#N/A	#N/A	#N/A	59	22	90	65	60	80	73,75
#N/A	#N/A	#N/A	#N/A	50	14	95	110	115	120	110
#N/A	#N/A	#N/A	#N/A	76	1	80	85	90	95	87,5
#N/A	#N/A	#N/A	#N/A	63	25	70	70	60	60	65

pre_L_AC_0	pre_L_AC_1	pre_L_AC_2	pre_L_AC_4	pre_L_AC_m	pre_AWRS	pre_AWRS_H	pre_CAP	pre_dewa_A	Diff_CAP	Diff_AC
105	110	80	95	97,5	0	0,1	1	0,5	3	70
85	90	85	90	87,5	0	0,1	7	0,5	#N/A	#N/A
70	80	90	120	90	0	0	#N/A	0,4	#N/A	55
65	65	70	75	68,75	0	0	7	0,7	0	42,5
70	90	105	110	93,75	0	0,3	6	0,6	0	78,75
40	105	110	95	87,5	0	0,1	7	0,5	0	72,5
80	120	120	120	110	0	0,1	4	0,2	3	72,5
80	70	55	75	70	0	0,3	4	0,3	1	41,25
70	90	100	105	91,25	0	0,4	7	0,6	0	61,25
40	85	115	115	88,75	0	0	5	0,7	#N/A	#N/A
100	115	120	120	113,75	0	0	5	0,1	0	80
120	120	120	120	120	0	0	4	0,3	0	78,75
25	85	120	120	87,5	0,1	0,3	5	0,7	0	31,25
65	80	90	80	78,75	0	0	4	0,5	1	43,75
50	65	70	80	66,25	0,1	0,9	6	0,9	-1	82,5
65	85	100	105	88,75	0	0,4	5	0,9	#N/A	#N/A
95	105	105	100	101,25	0	0,3	7	0,6	#N/A	#N/A
110	100	105	100	103,75	0	0,4	2	0,2	4	#N/A
80	90	120	120	102,5	0	0,3	#N/A	#N/A	#N/A	#N/A
85	85	90	100	90	0	0,3	6	0,6	#N/A	62,5
100	90	85	95	92,5	0	0,2	5	0,4	2	70
95	85	85	115	95	0	0,1	1	0,5	6	81,25
115	100	110	105	107,5	0	0	1	0,1	6	73,75
90	90	95	120	98,75	0	0,2	5	0,5	0	77,5
100	90	75	75	85	0	0,1	7	0,5	0	101,25
45	90	120	120	93,75	0,2	0,5	5	0,7	0	62,5
120	120	120	120	120	0	0	3	#N/A	#N/A	95
65	70	100	120	88,75	0	0,5	5	0,8	1	20
85	85	90	120	95	0	0	5	0,5	#N/A	47,5
120	120	120	120	120	0	0,2	5	0,5	0	55
60	65	65	75	66,25	0	0,4	5	0,7	1	52,5
85	85	90	80	85	0	0,1	4	0,3	#N/A	51,25
120	115	120	120	118,75	0	0,1	4	0,5	1	90

95	105	100	90	97,5	0	0	1	#N/A	4	67,5
60	75	75	75	71,25	0	0,3	4	0,6	1	45
75	65	70	80	72,5	0	0	#N/A	0,1	#N/A	41,25
100	105	100	115	105	0	0	0	0,1	#N/A	71,25
75	70	75	90	77,5	0	0,3	5	0,6	2	50
90	105	95	100	97,5	0	0	5	0,3	2	50
50	65	85	95	73,75	0	0,1	5	0,3	#N/A	36,25
60	70	75	120	81,25	0	0,6	#N/A	#N/A	#N/A	57,5
95	95	85	70	86,25	0	0	4	0,5	1	51,25
55	100	120	120	98,75	0	0	4	0,3	#N/A	65
85	80	85	120	92,5	0	0,1	6	0,7	0	86,25
110	110	75	90	96,25	0	0,4	6	0,3	#N/A	56,25
105	100	95	120	105	0	0	3	0,5	2	56,25
65	100	120	120	101,25	0	0	4	0,6	3	90
70	95	95	90	87,5	0	0,2	7	0,7	0	78,75
65	85	80	85	78,75	0	0,4	7	0,5	0	58,75
120	120	120	120	120	0	0,3	5	0,4	2	46,25
100	110	110	110	107,5	0	0,1	4	0,5	3	73,75
80	85	90	85	85	0	0,1	7	0,3	0	57,5
120	120	120	120	120	0	0,1	1	0,1	6	37,5

Diff_dewa	#N/A
-0,4	-0,1
#N/A	#N/A
#N/A	#N/A
0	-0,3
0,1	0,1
0	#N/A
0,3	#N/A
0,4	0
0,2	#N/A
#N/A	0
0,5	#N/A
#N/A	0,1
#N/A	0,1
#N/A	0
-0,1	#N/A
#N/A	0,1
#N/A	-0,1
0,2	0
#N/A	0,5
0,1	
0	
-0,1	
0,2	
-0,2	
0,3	
-0,3	
#N/A	
-0,6	
0	
-0,1	
-0,1	
#N/A	
0	

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École polytechnique de Louvain

Rue Archimède, 1 bte L6.11.01, 1348 Louvain-la-Neuve, Belgique | www.uclouvain.be/epl