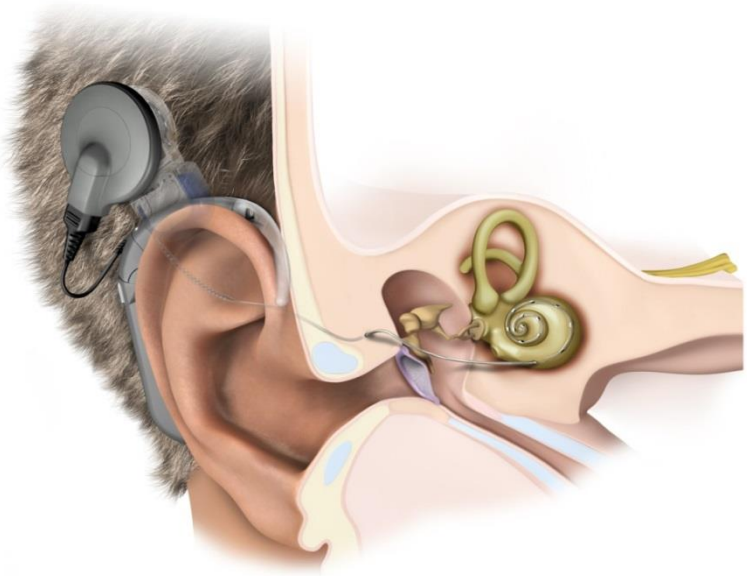
# Periodic Report Year 2

*Major achievements during the 2nd reporting period*

*1 October 2014 – 30 September 2015*



**EU project ID 611230**

# 1 About ACTION

## ACTive Implant for Optoacoustic Natural sound enhancement

The aim of the project is to develop a novel type of cochlear implant; a medical device used to restore auditory sensations for hearing-impaired listeners. An important part of the implant is the electrode, which is placed into the inner ear, also known as the cochlear. Currently available solutions use electric stimulation to generate a signal in the spiral ganglion neurons. ACTION will instead use optoacoustic stimulation to trigger the available residual hair cells. To this end, very small lasers - so called VCSELs - will be placed in the cochlear to stimulate the hair cells using the optoacoustic effect.

ACTION is a collaborative research project of seven partners. The project is funded by the Seventh Framework Programme (FP7) of the European Union and it runs under the Project **ID 611230** within the funding scheme "Small or medium-scale focused research project (STREP)". It is part of the work programme topic: Objective ICT-2013.3.3 3.3 Heterogeneous Integration and take-up of Key Enabling Technologies for Components and Systems.

The project started on 1 October 2013 and runs for a period of 36 months until September 2016.

## 2 Introduction

Traditional cochlear implants are based on the concept of electrically stimulating nerve fibres. Put simply, an electric field is generated inside the cochlea, which causes the nerve fibres to send a signal to the brain. Our brains interpret this signal as sound.

The geometric conditions inside the cochlea limit the options to focus the electric field. Since the cochlea has a tonotopic structure, targeting one specific tone usually triggers others as well. This may lead to a reduction of the quality of hearing. Some CI users retain hearing in the low frequency region and can use a special speech processor including a hearing aid. However this requires an earmould to be used, which is not always acceptable to the recipient. Use of the implantable laser developed in this project will allow sound transmission without an earmould.

Essentially, the so-called opto-acoustic stimulation can be explained as follows: The laser, which is placed inside the cochlea, generates a very short pulse of infrared light. The pulse is absorbed by the liquid inside the cochlea. This causes the absorbing local portion of the liquid to heat up and, consequently, expand rapidly. This expansion creates a sound wave, which travels through the cochlea. The opto-acoustic stimulation is similar to natural hearing, which relies on a sound wave being generated by the stapes pushing against the oval window at the base of the cochlea.

# 3 Major Technical Achievements in Year 2

## 3.1 System Overview

Laser-based stimulation requires research in and development of various components which need to be combined to a device. These components are (see also Figure 1): miniature laser source (i.e. VCSEL), collimating optics (i.e. lens), hermetic and biocompatible micro-package, biocompatible lead (i.e. flex), anti-fouling protection, signal generation electronics, firmware and software, and more. Furthermore, research into the actual optoacoustic effect, development of stimulation patterns and investigation of efficacy and safety are needed. The project relies on the expertise of its members in the fields of medicine, biology, chemistry, implant technology, laser technology, electronics, optics and packaging. The following subsections describe the progress in the respective fields in the past year.

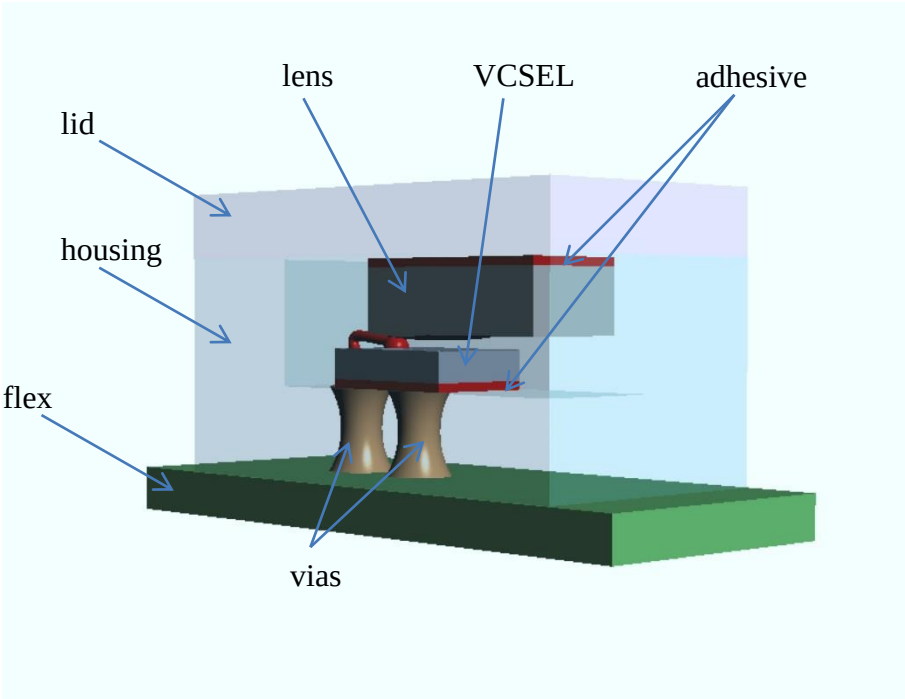



**Figure 1: Major components of the implantable laser source. The vias are electrical feedthroughs, which provide electric current to the VCSEL inside the hermetic package (i.e. housing and lid).**

## 3.2 Optical System Development

VERTILAS finalised the design for the custom made VCSEL arrays operating at 1550 nm wavelength and completed the fabrication of the first wafer. Figure 2 shows several VCSEL arrays after asymmetric laser dicing to produce dice with a minimal dicing border. The chips show no vertically protruding dicing burrs which are characteristic for standard saw-dicing processes. These burrs can reach 10 µm in height and could potentially interfere with the subsequent lens alignment procedure.

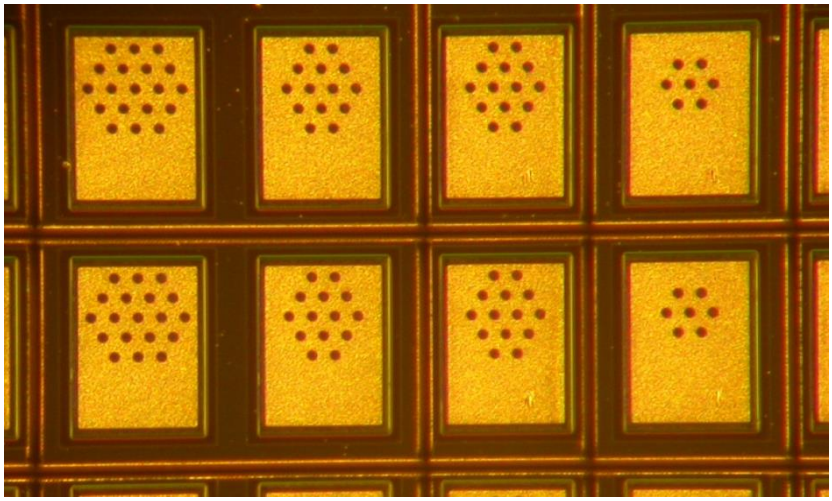


**Figure 2: Laser diced 1550 nm VCSEL arrays showing a hexagonal geometry with a 50 µm pitch between apertures. The dicing lines are not in the centre of the dicing street but rather laterally offset toward some VCSELs to minimise the dicing boarder.**

SUSS designed and fabricated Si-lenses to collimate the VCSEL light. There is indication that higher intensity light is more likely to generate a sound wave in the cochlea fluid (or any fluid for that matter with absorption in the right range). Figure 3 shows a section of the wafer with microlenses and alignment features. The lens is 15 µm high and the underlying slab of silicon is polished down to 150 µm.
VCSEL and lens are made of non-biocompatible materials. In order to protect the devices from the harsh environment of the body and to protect the body from potentially toxic materials, VCSEL and lens have to be hermetically sealed. The packaging approach is described in the next subsection.

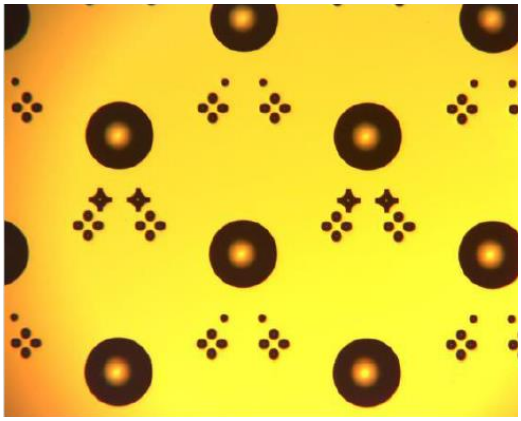


**Figure 3: Single micro-lens developed and fabricated by SUSS before dicing. The lens is 15 µm high and the underlying slab has been polished down to 150 µm.**

## 3.3 Packaging and Fabrication Process

Development of a hermetic medical micro-package at CSEM has progressed considerably in the past year. Figure 4 (left) is a micrograph of a hermetic micro-package made of sapphire. The VCSEL can be seen inside the cavity. The laser-assisted bonding process of lid and housing generates very little heat and does not damage the VCSEL or other potential electronic components inside.
Figure 4 (right) is a photograph of a novel flexible substrate made of platinum and silicone. All process steps are designed with automation/batch processes in mind in order to reduce manufacturing costs while, at the same time, improving its mechanical properties with off-the-shelf implantable leads or substrates.

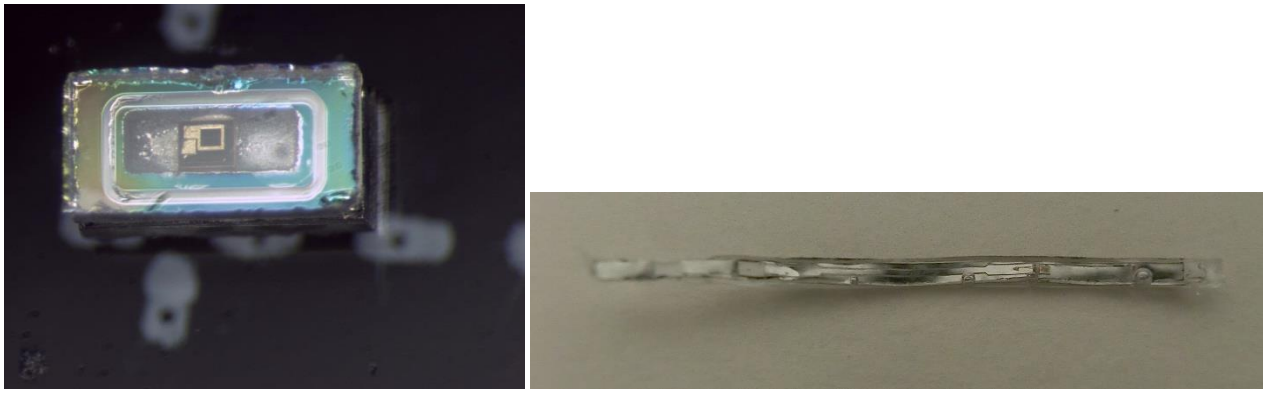


**Figure 4: Left: Hermetic package made from sapphire with a length of 1.5 mm and a width of 0.6 mm. The VCSEL can be seen in the cavity of the package. Right: Flexible substrate made of platinum and silicone. The device is 22 mm long and ~0.8 mm wide.**

As we could not wait for the micro-packages to run tests on the VCSEL and lenses, ST-I designed and CSEM fabricated a non-biocompatible version of the optical cochlear implant. These are called System A. We have now made mark three of this device (called System A++), which integrates the new VCSEL and the Si-based lens on a flexible polyimide substrate. Figure 5 shows a micrograph of System A++. The lens, appearing blue, is bonded directly on top of the VCSEL. A wire bond connects the top pad with the metal lines of the substrate. The entire device is overmoulded with silicone to protect the components and to improve its mechanical properties for better handling during tests.

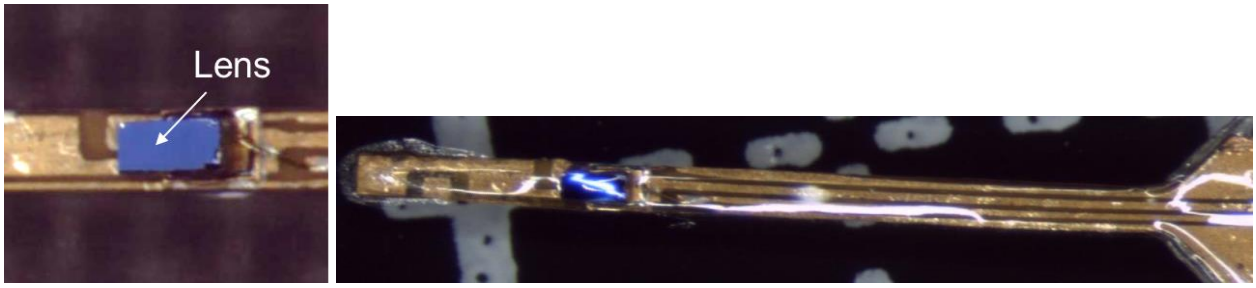



**Figure 5: Micrographs of System A++. Left: Close up of the VCSEL and the lens (blue) bonded to the polyimide substrate. Right: The tip of the substrate has a width of ~0.4 mm. After ~10 mm, it widens to provide better handling during tests.**

## 3.4 Antifouling Coatings

Antifouling coating studies at VTT continued with developments to further understand the antimicrobial activity of thin films deposited by atomic layer deposition (ALD). New types of coatings were prepared and the stability of the coatings was studied in terms of the adhesion and crack resistance of $Al_2O_3$ on soft PDMS encapsulant planned to be used in the final device. In parallel, sol-gel coatings containing quaternary ammonium groups for antimicrobial performance and polyethylene oxide (PEO) segments are being investigated in tests as an alternative.

Thin films in the project have been analysed by common surface analysis and imaging techniques. The antimicrobial activity has been determined on heat sterilized samples (160°C, 4h) followed by incubation at 37°C (24 - 48 hours). Then the number of viable bacteria was analysed by plate count analysis, and by epifluorescence microscopy on samples stained with acridine orange. The antifouling characteristics of the films were further studied by QCM-D in protein adhesion studies using Bovine serum albumin (BSA) at 0.2 mg/ml concentration in 0.85% NaCl.

Our findings for this year include:

- Characterisation and testing of ALD deposited thin silver films for biomaterial applications
- Improved understanding of the effects of ALD coated $Al_2O_3$ and other thin film in biomaterial applications in terms of potential leachates
- Comparison of ALD thin films with commonly used quaternary and PEO surface functionalized samples (ongoing)

Silver was deposited by ALD on 50nm $TiO_2$ following literature procedures, and displayed excellent antimicrobial activity (Table 1). Protein adhesion studies showed that both silver and $SiO_2$ bind approximately 600ng/cm$^2$ BSA; however, further investigations revealed that functionalization of the silver surface with a self-assembled monolayer of thiophenol (originally deposited to minimize oxidation) led to lower BSA adsorption levels (450ng/cm$^2$). Transmittance in the infrared range proved to be remarkably high for 4 nm silver coatings on $TiO_2$ layers, deposited on top of a borosilicate glass substrate (see Figure 6).

| Film type | Description | Log colony forming units cm$^{-2}$ |
|---|---|---|
| Silicon | 50nm TiO2+ 4nm Ag, (TiO2-Ag) | < 1 |
| Silicon | 50nm TiO2+ 4nm Ag + thiophenol (TiO2-Ag-TF) | < 1 |
| Uncoated silicon | | 3.1±0.5 |
| Glass | 50 nm TiO2+ 4 nm Ag (TiO2-Ag) | <1 |
| Glass | 50nm TiO2+ 4nm Ag + thiophenol (TiO2-Ag-TF) | < 1 |
| Uncoated glass | | 4.3 ±0.1 |

**Table 1: Number of viable bacterial cells (Log colony forming units cm$^{-2}$) on sample surfaces after one day exposure.**

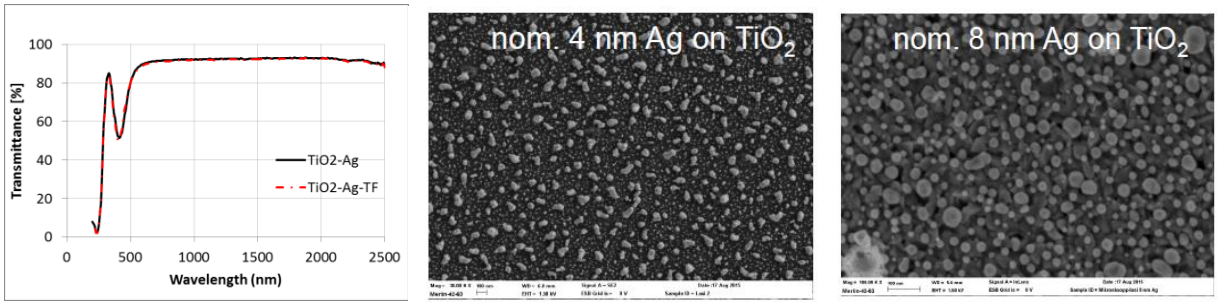



**Figure 6: The IR-Vis transmission spectra and SEM images of Ag coatings on borosilicate glass (TF = thiophenol).**

## 3.5 Stimulation Platform Integration

The work that has to be pursued in the WP4 aims to realize a stimulation platform that lays the groundwork for a potentially human-semi-implantable system, with efforts that will focus on the development of a miniaturized implantable VCSEL driver, pre-processing electronics for large area neurostimulation and recording, decision making, communication and energy management functionalities. Namely the constituting parts of the stimulation platform are:

- A miniaturized VCSEL driver and pre-processing electronics for optical neurostimulation and recording
- Development of an extra-corporal device containing a user interface, decision making, communication and energy management functionalities base station

The VCSEL driver PCB was designed, manufactured and tested by ST-I, MED-EL and CSEM in the second year of the project. Figure 7 is a photograph of the PCB. It has a size of 36 mm x 80 mm.

The VCSEL driver electronics has to be characterised with regard to three aspects: First the verification of the driver capability with regard to laser current amplitude and laser current slew rate, second the examination of the influence of the flexible interconnect transmission lines on the laser current slew rate, and third the optimization of the impedance matching circuit. First measurements (Figure 8) of the optical output power indicate, that the long metal lines (~100 mm) have little influence on the rise time of the output signal.

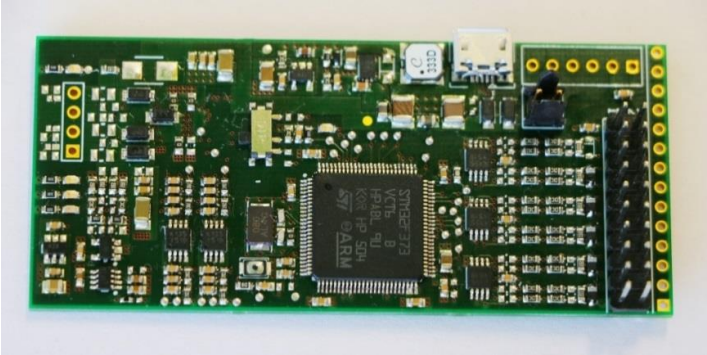


**Figure 7: VCSEL driver PCB for system B with a size of 36 mm x 80 mm.**

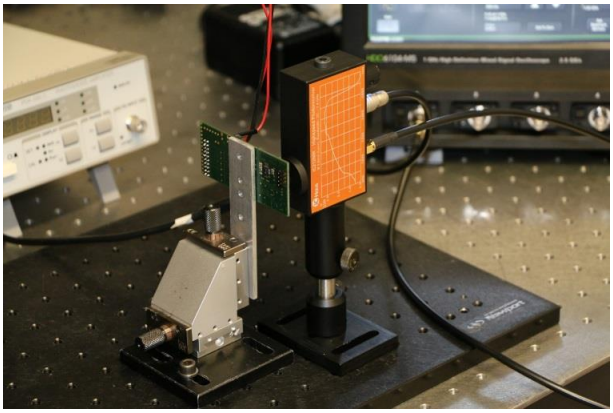


**Figure 8: VCSEL driver test setup with driver board, photo receiver (orange) and high speed oscilloscope in the background.**

## 3.6 Implant Studies

Previously, tests with our early System A did not create powerful sound waves in saline. These are too weak to generate oaCAPs. The reason is that the pulse length was limited to 1 µs. As the flexible substrate of System A is not an ideal heat sink, the VCSEL starts to heat up, causing the optical output power to decrease after ~100 ns and, eventually, drop to zero within 2 ms (see Figure 9, 1 µs pulse). Permanent and repeated internal heating might damage the VCSEL and reduce its lifetime dramatically. Reliability tests will be run to quantify its lifetime.

Measurements at MHH show that optical pulses with sufficient power and energy will produce an oaCAP, but there is a threshold for both. So far, the shortness of pulses produced with the VCSEL (1 µs) have not generated an oaCAP, as can be seen in Figure 10. Longer pulses or trains of clicks will have to be tested to see if the threshold in energy can be overcome. Furthermore, future devices will contain a microlens which collimates the laser beam leading to a higher energy and power density. Measurements shown in Figure 10 also reveal that the high electric currents of up to 200 mA generate an electric artefact. Fortunately, this signal occurs before the expected oaCAP and can, therefore, be filtered.

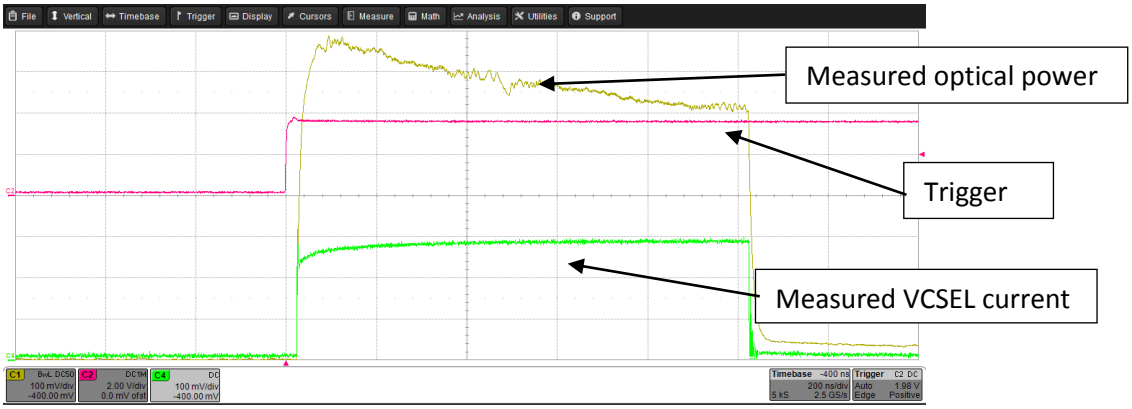



**Figure 9: Measured optical output power of the VCSEL for a 1000 ns pulse. Peak power is reached after ~50 ns and starts to decrease due to internal heating of the VCSEL and insufficient heat sinking.**

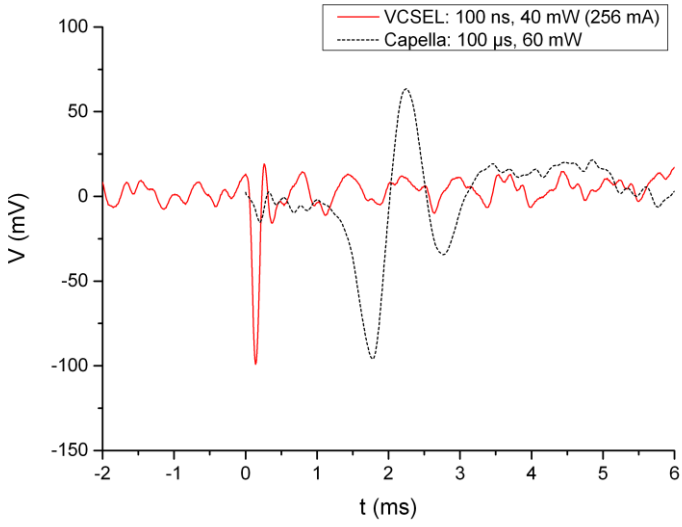



**Figure 10: Comparison of the artefact (in red) with an optically evoked CAP (in black), generated with the Capella laser system. In both measurements the laser pulse was applied at t = 0 and an amplification factor of 10000 was used.**

# 4 Outlook for Year 3

At the core of our future activities will be the measurement of an oaCAP generated by the VCSEL. Higher pulse power and/or longer pulses will be required. Optimised heat dissipation should help keep the VCSEL cool for a longer time, raising the possibility to run the VCSEL for longer without damaging it.

The VCSEL driver and new software will allow us to test new alternative stimulation patterns. They could help us overcome the energy threshold for an oaCAP. Investigating these aspects requires the joint effort of all members of the consortium.

Optical output from System A++ will have to be characterised to measure the performance of the collimating lens. New devices with VCSELs at 1850 nm wavelength will be assembled and combined with the Si-based lenses to measure their performances as well.

Furthermore, we will have to prove that our micro-packages are hermetic and remain so for the lifetime of a cochlear implant, which can be as much as 70 years. The electric feedthroughs will be the focus of our attention.

Antifouling coatings will have to prove to be crack-resistant on soft flexible materials such as silicone (with PDMS as one of its more prominent members).

On the electronics side, we will strive to further improve the driver hardware and software and integrate all components in a short-term implantable device with external electronic parts.