

# A Novel System For Monitoring Organs For Transplant

A monitoring system whose core element is a silicon-based, needle-shaped microsensor has been developed to continuously monitor organ status during the transportation phase of a transplantation process.<sup>1</sup> The result of a multidisciplinary research project, its development is expected to lead to devices for several new application niches.

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Image: PhotoDisc

## Assessing organ viability

Under current transplantation protocols, one of the most critical and unaddressed phases of the transplant process is organ transportation from donor to recipient, during which the elapsed time and preserving conditions must be thoroughly controlled. In this phase, the organ remains immersed in a sterile, organ-preservation solution at a temperature of 2–8 °C. During this time, it is essential to maintain organ viability to ensure the complete restoration of organ function following transplantation.

Paradoxically, direct evaluation of organ function after transplantation

is, to date, the only reliable procedure for the assessment of correct preservation during transportation. Although some viability indicators have been proposed and tested such as nucleotides, energetic charge and histology they are extremely invasive (requiring various tissue biopsies) and time-consuming (imposing a considerable time lag that can stretch out to a couple of days). Therefore, these indicators are seldom used in clinical practice and have been mostly relegated to experimental studies.

Although some alternative indicators such as pH, [K+] and tissue impedance have been proposed for immediate assessment of organ viability, experimental results suggest that these parameters must be used in a continuous monitoring scheme to accurately predict organ viability.<sup>2,3</sup> This presents a conundrum because current monitoring systems are markedly unfit for monitoring organ-transport conditions.

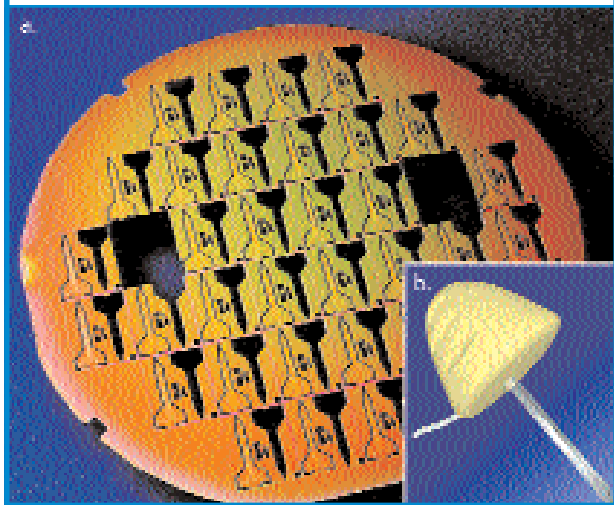
## The need

The lack of proper methods for assessing organ viability creates an undesirable gap in the costly and otherwise carefully devised protocol of organ transplantation. Thus, when an organ reaches the recipient, the main criteria for proceeding with implantation are the observance of standard ranges of transport time and a visual inspection by an expert

surgeon. This crude evaluation protocol does not take into account any incidents that may have arisen during transportation or the inherent variability in the response of organs to sustained ischaemia during transportation. The problem becomes aggravated by a growing tendency to make use of suboptimal organs. As transplantation demand peaks in developed countries, donor numbers remain essentially stuck. This has motivated health-care institutions to approve transplantation of organs coming from “nonheart-beating,” that is, cadaveric, donors, which present, from the outset, doubtful and handicapped viability.

These converging factors create a burgeoning demand for an objective and practicable organ-viability indicator during the transportation phase. The system that is presented in this article provides the means for doing this by way of continuous, minimally invasive monitoring of tissue impedance and temperature. Exploiting available technology, the system can be seamlessly integrated into a transportation cool-box, providing medical practitioners with an easy-to-use, reliable indicator of organ viability that could boost the number of successful transplantations and available donors, while shrinking the ratio of viable organs that are now discarded for safety reasons. →

**Figure 1:** The microprobe multisensor. a) Image of a Si wafer after the fabrication process used to make the microprobe  
b) Final packaging design of the microprobe



### → Measuring principles

Available microsystems and microelectronics technologies allow the integration of a large variety of sensors on a single substrate. These sensors can be chemical or physical and present reliable characteristics. The first step in work to develop the monitoring device was determining which physicochemical tissue parameters (among the many that can be measured using silicon microsensors) would be useful for establishing an organ-viability criterion. As mentioned, tissue impedance, pH and  $[K^+]$  have been proposed as feasible indicators of organ viability by continuous monitoring, but reliable data on their clinical usefulness was scant and limited by the use of invasive, macroscopic sensors. Therefore, the usefulness of these different parameters (correlated with temperature for normalisation) was examined in a standard organ transportation protocol using custom-developed microprobes. The results showed that, although a priori biologically and technically viable, the pH and  $[K^+]$  microprobes presented numerous problems. These problems are related to the need for a reliable and miniaturised reference electrode and systematic calibration before use. In the light of this, tissue impedance microsensors (normalised with temperature readings) emerged as the best option for assessing organ viability on a continuous monitoring basis. Not only do they eliminate the need for a reference electrode, but also they provide the means for inferring information on organ viability, supplied by  $[K^+]$  and pH microsensors.

### System integration

A  $9 \times 0.6 \times 0.5 \text{ mm}^3$  multisensor microprobe containing temperature and impedance sensors was selected (Figure 1).<sup>4</sup> In the context of the organ transport application, this microprobe made up the core of a disposable system ( $10 \times 5 \times 1.5 \text{ cm}^3$ ) that holds the electronics for data acquisition, preprocessing and a short-distance telemetry unit, and which is placed besides the monitored organ inside a cool-box during

transportation to report on its preservation status. The disposable unit transmits monitoring data to an external personal device assistant (PDA); a number are on the market, the PALM 515m is used here. The PDA is located on the cool-box lid and can be easily handled by the medical staff. Monitoring data are recorded and displayed on the PDA once per second, and the PDA log can be downloaded to a PC mainframe on arrival of the cool-box at a medical centre for more detailed evaluation of organ status.

### Prototype

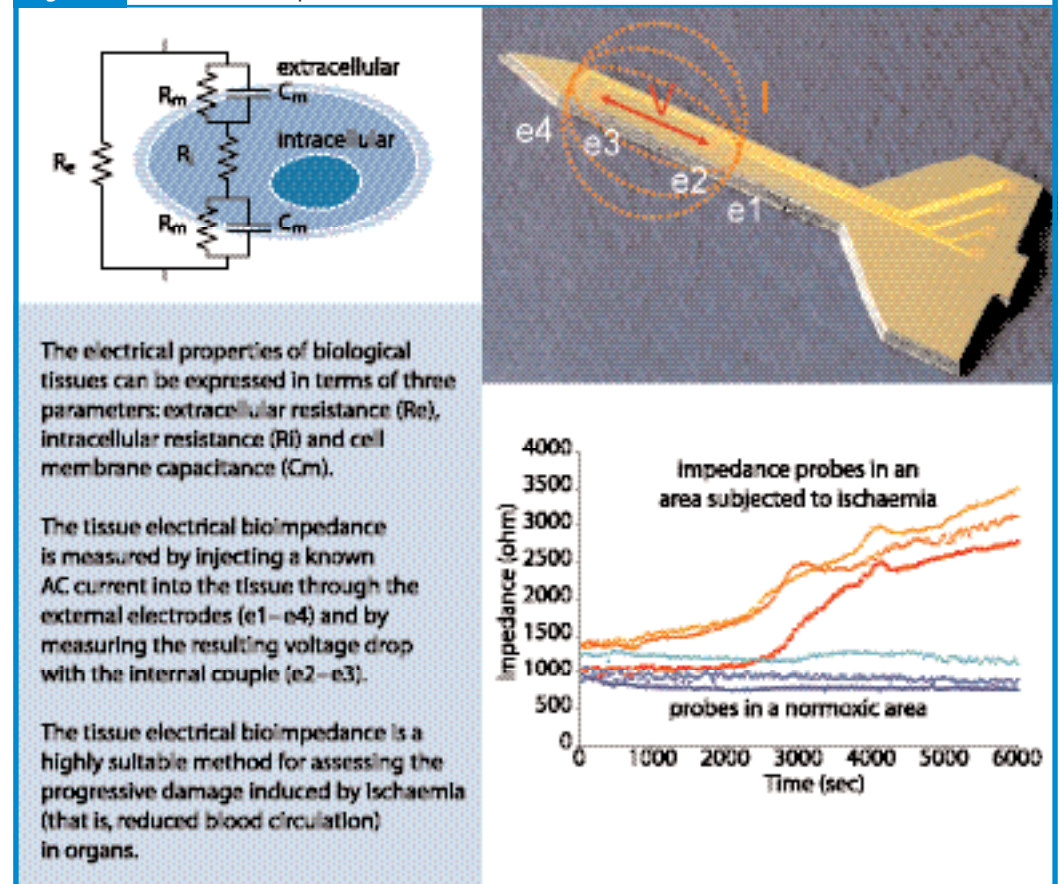
Carbueros Metálicos SA (Air Products)<sup>5</sup> participated in the European Community research project<sup>1</sup> and currently owns the exploitation rights of the multiprobe microsensor patent. The company contracted Industrial Innovation Microelectronics Design SA (i2m)<sup>6</sup> to fabricate an industrial prototype to be tested in a real-life clinical environment. i2m is

also working in close collaboration with the National Centre of Microelectronics of Barcelona<sup>7</sup> to improve the encapsulation technique and thereby reduce fabrication costs and to obtain the CE mark for the device. The complete system could be ready for commercialisation in approximately two years.

### Innovation

The impedance characteristic of preserved organs is specific to each organ (Figure 2). In general, after organ extraction, the impedance increases because of a decrease in extracellular fluid, generalised cellular swelling and closure of gap junctions. Thereafter, impedance remains stable for 1–2 hours; beyond this it starts decreasing as a result of massive membrane breakdown. Experimental data show that this rise in impedance appears earlier in heart tissue and later in liver and kidney tissues. This is in agreement with the established clinical fact that

Figure 2: What is the bioimpedance?



kidneys are longer-lasting organs than hearts and livers. Moreover, experimental studies with animal organs have also demonstrated a significant correlation with the energetic charge value of tissue biopsies. This further strengthens the case of tissular impedance monitoring as a reliable indicator of organ viability.

When impedance values beyond the standard range are detected, the system sets off alarms to inform the medical team of the risky organ status. This information can be used to adjust the cool-box temperature during transportation and on arrival at the medical centre the medical practitioners possess additional information for decision-making at the time of implantation.

## Summary

It has been established in animal tests that this monitoring can be used as a reliable indicator of organ viability prior to implantation. The complete system has an easy-to-use interface, integrates seamlessly in a transport cool-box and conducts continuous, minimally invasive monitoring of the organ, making it a suitable tool for its intended clinical application. The system constitutes the starting point of a new line of equipment that, using custom multiprobe microsensors as core elements, will prompt the path towards new biomedical application niches in the field of microsystems.

## Acknowledgement

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