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EDITORIAL

Four-terminal impedance monitoring of cardiac output: an elegant clinical application of a classical engineering trick

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This editorial refers to 'Intracardiac impedance monitors stroke volume in resynchronization therapy patients' by M. Bocchiardo *et al.*, on page 702.

Nothing is more basic to life than cardiac output. However, an accurate method to monitor cardiac output with an implantable device has long eluded device developers. In this issue of the Journal, Bocchiardo *et al.*[1] present significant progress toward that end with encouraging human data.

Background

Electrical impedance is defined as the ratio of voltage (across) to current (through an object). This is typically measured by a two-terminal method. With the two-terminal method, the same contacts are used to inject the current and measure the voltage (or, equivalently, to impress the voltage and measure the current). This works quite well for most electronic components such as a discrete resistor found at an electronics store. However, in a fluid medium, the two-terminal method can introduce significant errors.

Consider a glass aquarium filled with blood that is 20 cm long with a cross section of 10 × 10 cm (giving the cross-sectional area of 100 cm^2). With the typical bulk resistivity of 150 Ωcm for blood the resistance, from end to end, of the blood will be:

$$30\ \Omega = \frac{150\ \Omega\,\text{cm} \bullet 20\ \text{cm}}{100\ \text{cm}^2}$$

Now imagine that we attempt to measure the impedance using 2 mm diameter (1 mm radius) electrodes. The impedance from the electrode to the nearest 1 cm (10 mm) of fluid may be calculated by summing the resistance of the spherical shells which each have a resistance of:

$$dz = \frac{\rho dr}{4\pi r^2}$$

where ρ is the resistivity of the fluid (150 Ωcm or 1500 Ωmm for blood) and r is the radius. The total resistance is then given by integrating from the 1 mm electrode radius to the 10 mm fluid shell radius.

$$Z = \int_1^{10} \frac{\rho dr}{4\pi r^2} = \frac{\rho}{4\pi}\left[\frac{1}{1} - \frac{1}{10}\right] = 107.4\,\Omega$$

Thus the resistance of just the first 1 cm of blood—from the small electrodes—is over 100 Ω each for a total of over 200 Ω. This significantly dominates the 30 Ω resistance of the whole blood chamber and thus provides material opportunities for static and dynamic errors.

This error is typically ignored when the only item of interest is the small resistance change from a modification of geometry of the tissue region. Such is the assumption with minute ventilation monitoring for physiologic pacemakers using a small pacing electrode as one of the resistance-sensing electrodes.

The problem is described, in engineering terms, by saying that the 'contact' resistance is large enough to introduce error into the measurement of the resistance of the object of interest. The engineering 'trick' to eliminate the contact resistance error is to eliminate the contact resistance by using different contacts for the current injection and the voltage measurement. In the blood-filled aquarium example, there would be a pair of electrodes at opposite ends of the length aquarium to inject the current. Another pair of electrodes, also at opposite ends—but not near the first pair—is used to sense the voltage across the length of the aquarium. The ratio of the voltage to the current is then the resistance.

Since there are four electrodes used, the measurement is referred to as a 'four-terminal' measurement. This is sometimes called a 'Kelvin' resistance measurement, and Kelvin described this technique in a paper on metallic resistance in 1857.[2] Kelvin was known as Thomson before he was knighted for his modifications of Maxwell's equations to explain the distortions in the signals emerging from the trans-Atlantic cables. These 'telegraph' equations were then used to explain propagation in long nerve

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axons. Coincidently, the light-mirror amplifier, used to amplify these weak trans-Atlantic signals, was used by Einthoven to record the first electrocardiogram. However, the Bavarian, Georg Ohm, first measured resistance in metallic wires long before there was such an instrument as the 'ohmmeter'.[3] Thus, it seems likely that he was forced to use a four-terminal measurement technique for his measurements.

The four-terminal resistance technique is very useful whenever the contact resistance is an appreciable fraction of the overall resistance—regardless of the contact size. Such is the case with external monitoring of cardiac output via resistance changes as invented by Kubicek and Patterson for the USA space agency NASA.[4] The thoracic resistance is low with high-voltage external defibrillation shocks. However, with low (tolerable) voltages, the epidermis presents a very high contact resistance. Hence, the external resistance monitoring of cardiac output uses a different set of electrodes for the current injection and the voltage measurement.

New results

In the present study, electrical current was injected between the right ventricular (RV) coil and RV pacing tip in patients with implantable cardioverter-defibrillators (ICD) and cardiac resynchronization therapy (CRT) devices. In other patients, the current was injected between the RV ring and tip electrodes. Due to the usage of the four-terminal approach, the significant resistance difference between the RV defibrillation coil and the smaller electrophysiology catheter ring were irrelevant. (There are some slight changes in the electrical field but those should have no first-order effects.)

The voltage was sensed between two electrodes in the left ventricular (LV) lead in the coronary sinus. This configuration should tend to be more sensitive to movement along the long cardiac axis, as the measurement axis is somewhat from the apex to the base of the LV. It would be interesting to see what the results would be from a more transverse vector. A similar configuration was used by some of the same authors in a canine study earlier although they used epicardial LV electrodes instead of transvenous electrodes.[5]

The mean correlation between the stroke resistance change (between end-systole vs. end-diastole) and the stroke volume was 0.82. While not accurate enough to be a substitute for laboratory thermal dilution measurements, this seems more than adequate for chronic monitoring for a possible loss of cardiac output from progression of heart failure. This, of course, assumes that these acute results are similar with chronic monitoring.

The correlations between the stroke resistance change and the pulse pressure were also high. This is to be expected, as the pulse pressure correlates with the stroke volume—for a fixed arterial load—in keeping with the haemodynamic analogue of Ohm's law. In the case of vasodilation, one would hope that the stroke resistance change would still correlate with the stroke volume as the stroke volume is directly tied to the blood pool volume and geometry somewhat independently of the arterial load.

This study was limited to patients with non-ischaemic cardiomyopathy, but it seems reasonable that similar results would be seen with infarction patients. Calibration may be more individualized depending on the location of significant wall-motion abnormalities. It is interesting that one of 14 patients had a very low correlation of only 0.26. This suggests that the approach may not be applicable to every patient. Future work may allow the determination of patients with such poor correlations.

A reasonably accurate method of continuous cardiac output monitoring may offer utility well beyond heart failure monitoring and CRT timing adjustments. For example, aggressive anti-tachycardia pacing therapy for high-rate tachycardias could be implemented with more confidence if it was known that adequate cardiac output was present. There have been encouraging results with so-called 'medium voltage' electrical therapies to generate cardiac output in spite of ongoing VF as seen with storm.[6] Medium voltage therapy may show promise for treating pulseless electrical activity (PEA).[7] Since the detection of PEA is not possible with a purely electrogram analysis, the addition of a reliable estimate of cardiac output is required. The four-terminal resistance approach of the new study may be the answer.

The authors are to be congratulated for their preliminary demonstration—in humans—of what may be a significant development in the long search for an implantable cardiac output monitor.

Conflict of interest: M.W.K. has received speaking honoraria from St. Jude Medical and is a director of Galvani Ltd.

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