Revealing the patterns at the heart of life and death

Dynamical instabilities that cause specific patterns of electrical activity in the heart wall are intimately connected to cardiac arrest, the largest cause of death in the developed world. This is one of the key observations of research reported by Sitalika Sinha and Johannes Breuer of the Institute of Mathematical Sciences in Chennai. Their work could lead to the design of a safer kind of implantable cardioverter-defibrillator (ICD).

The normal rhythmic contraction of the heart muscles is triggered by waves of electrical excitation that propagate through the cardiac tissue. The frequency of the cardiac rhythm is usually determined by the sinus node, a specialized group of self-excitatory cells in the upper right chamber of the heart, which generates these waves.

However, where the heart is diseased or deformed, the normal rhythmic activity can be disrupted. Such a malfunction, called arrhythmia, may be experienced even by healthy people from time to time, felt as a skipped or fluttering heartbeat.

There are more dangerous arrhythmias, such as ventricular tachycardia (VT), which occurs in the lower chambers of the heart. During VT the heartbeat becomes abnormally rapid, with as many as 200 beats per minute. If episodes of VT occur for very brief periods, they are usually harmless, despite causing the heart to pump inefficiently. But sustained periods of VT are dangerous and, unless treated, are potentially fatal.

The most common mechanism for VT is the formation of a re-entrant pathway. This is a closed path of excitation feedback, or short-circuit, with the excitation wave going round and round an existing inexcitable obstacle such as a scar tissue (Fig. 1).

For people with a chronic risk of VT, the preferred treatment is to have an ICD implanted. This is a device that can detect the onset of such arrhythmias and provide in response an appropriate sequence of periodic low-amplitude electrical stimuli (referred to as pacing) through an electrode, usually placed in the ventricular apex.

Figure 1 Ringing the changes. Traditional one-dimensional model of ventricular tachycardia showing an excitation wave going round an obstacle such as scar tissue.

The device operates on the principle that by pacing at a frequency greater than that of the VT, the stimulated waves will eventually reach the re-entrant circuit and terminate the re-entry, thereby restoring the normal activity of the heart.

However, the underlying mechanisms of the success and failure of pacing termination are not yet well understood, and the algorithms currently used in such devices are often based on purely heuristic principles," says Sinha.

"As a result, occasionally, instead of terminating VT, pacing can accelerate it or even promote its degeneration to lethal ventricular fibrillation, leading to death within minutes if no immediate action is taken," he explains. "Understanding the interaction between pacing and re-entrant waves is therefore essential for designing more effective and safer ICD pacing algorithms."

At the moment, the only way to save a patient whose heart is fibrillating is to apply a very high-voltage electrical shock to the heart, a process known as defibrillation. This treatment is not only extremely painful, but can in many cases cause further damage to heart tissue, says Sinha.

Current theoretical studies of pacing consider re-entry in a ring of cardiac cells. Because the ring is a line of cells, it is only one-dimensional, even though the propagation of excitation in the heart occurs in a three-dimensional tissue. The conventional view is that each pacing wave splits into two branches in the re-entry circuit, the retrograde branch travelling in the opposite direction to the re-entrant wave and, eventually colliding with it, the waves then annihilating each other. The other, anterograde, branch travels in the same direction as the re-entrant wave and, depending on the timing of the pacing stimulation, either resets the re-entry by becoming the new re-entrant wave, or leads to termination if it is blocked by a refractory region left behind in the...
wake of the preceding wave. Sinha says that these arguments break down beyond the one-dimensional ring geometry.

Sinha has been focusing on research aimed at designing more effective and safer ICD pacing algorithms by refining and using more realistic two-dimensional models of heart tissue. Using such models, his earlier studies have shown that the existence of inhomogeneities in the re-entry circuit are required for the successful termination of VT by pacing.

More recently, Sinha and Breuer, a student from the Technical University Berlin in Germany, who has been working with Sinha in Chennai on an exchange programme, have shown that the nonlinear conduction properties of cardiac tissue can lead to a pattern-formation instability that plays a vital role in the pacing treatment of tachycardia.

Their latest results show that the generation of waveform modulations through dynamical instabilities, as a result of restitution and dispersion effects in cardiac tissue, leads to the formation of conduction inhomogeneities in the re-entry circuit (Fig. 2). "This disorder in turn leads to conduction block during rapid pacing and therefore results in successful re-entry termination," they report.

Based on the results of simulations, the pair conclude that the various pacing parameters have to satisfy certain constraints for successful re-entry termination. For example, the pacing interval has to be shorter than the re-entry period, but it cannot be too short because the propagation of high-frequency waves causes instability, causing the wave to break up. In addition, the number of pacing stimuli has to be high enough but not so high that it causes additional conduction blocks, which would restart the re-entry.

"This shows that designing an optimal pacing algorithm is essentially a complex optimization problem," they say, adding that their findings could be applied to the design of better pacing algorithms for ICDs.

The ultimate goal of anti-tachycardia pacing is to terminate re-entrant activity with stimuli of the smallest possible magnitude in the shortest possible time, with the lowest probability of giving rise to faster arrhythmias, Sinha told NewsIndia.

Breuer and Sinha (Fig. 3) caution that the constant-frequency pacing they investigated is only a partial solution to this problem, and that a more efficient algorithm might have to adjust the pacing intervals on a beat-to-beat basis. "Our investigation is aimed towards answering how such an optimized pacing scheme maybe designed," they add. In the future, pacing algorithms may work so well that they make defibrillating shocks obsolete, freeing cardiac patients from the constant fear of receiving such a painful treatment.


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Figure 2 Circuit-breaker. Dynamical instabilities can block the re-entry wave.

Figure 3 The dynamic duo: Johannes Breuer (left) and Sitabhra Sinha have studied the propagation of electrical activity in heart muscle.