

# Advances and new technologies in the treatment of atrial fibrillation

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## KEY POINTS

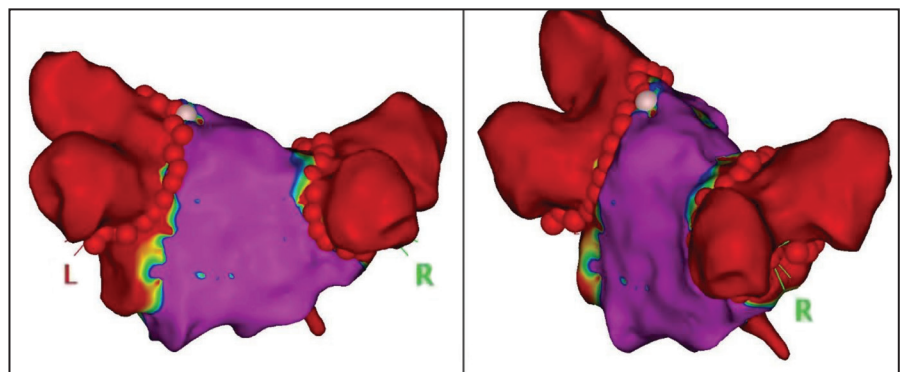
- ▶ Atrial fibrillation (AF) is a growing problem in Ireland.
- ▶ Wearable technology is leading to higher diagnosis rates.
- ▶ Restoration of sinus rhythm now has a Class 1A recommendation in the latest European Society of Cardiology (ESC) guidelines.
- ▶ Waiting lists lead to progression of early AF to more advanced forms.
- ▶ Catheter ablation techniques have improved rapidly over recent years, with significant reductions in procedure duration and fluoroscopy time.

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia worldwide<sup>1</sup> and is a growing problem in Ireland. The incidence and prevalence increases with age, and approximately one-in-four European adults over the age of 55 will develop AF.<sup>2</sup> Prevalence data from the Irish Longitudinal Study on Ageing (TILDA)<sup>3</sup> estimate the prevalence of AF at 3.2 per cent in Irish people over the age of 50, and using national population projections, this number is expected to increase three-fold to 107,000 by 2040.<sup>4</sup> The management of AF is no longer confined to cardiology, and is increasingly diffusing into multiple medical specialities.

Identification of modifiable risk factors (obesity, alcohol intake, physical inactivity) as well as treatment of concomitant diseases (hypertension, diabetes mellitus, obstructive sleep apnoea, heart failure) form a key part of the guidelines, and this holistic treatment approach reduces



**FIGURE 1:** Single lead ECG demonstrating AF. Generated with a hand held diagnostic device (KardiaMobile)



**FIGURE 2:** Voltage map of the left atrium following bilateral ablation of the pulmonary veins. Red indicates low voltage zones, with purple indication areas of preserved voltage. The red spheres indicate sites where ablation was performed

AF recurrence and improves symptoms.<sup>5</sup> This understanding, combined with technological advances, has improved the treatment options for AF significantly in recent years.

## Utilisation of wearable technology

The smoking gun that secures a diagnosis of AF is the ECG. However, in its paroxysmal form, capturing an ECG of AF can be difficult. Anecdotally we all know of patients who are troubled with daily palpitations, only to have a good day when a 24-hour ECG is connected and return 24 hours of sinus rhythm. The advancement of ubiquitous smart phones and smart watches now easily enables a

remote diagnosis, even when symptoms are infrequent.

Photoplethysmography (PPG) is a relatively simple optical technique that can detect blood volume changes in a microvasculature and estimate heart rate. Simply by using the camera on a smart phone, or PPG signal from a wearable fitness device (eg, Fitbit, Garmin), an estimation of heart rate can be given. To detect irregularity or abnormality however, a detection algorithm must be applied to the signal. The Apple Heart Study,<sup>6</sup> published in 2019, used a PPG detection algorithm to opportunistically screen over 400,000 participants. If an irregular

rhythm was detected, an ECG patch was sent to the participant and worn for seven days. When used simultaneously with the ECG, the positive predictive value of the PPG signal was 84 per cent, proving that population screening with this simple technique can work. In a smaller study, validation of a PPG algorithm achieved an accuracy of correctly identifying AF in 96 per cent of patients.<sup>7</sup>

Further advances in smart watch technology, and several commercially available hand-held portable devices, now enable an ECG rhythm strip (representing the standard lead I) to be generated from two electrodes collecting signals from the left and right limbs (Figure 1). The most recent ESC guidelines in 2020 now recognise a rhythm strip diagnosis of >30s to confirm a diagnosis of AF.

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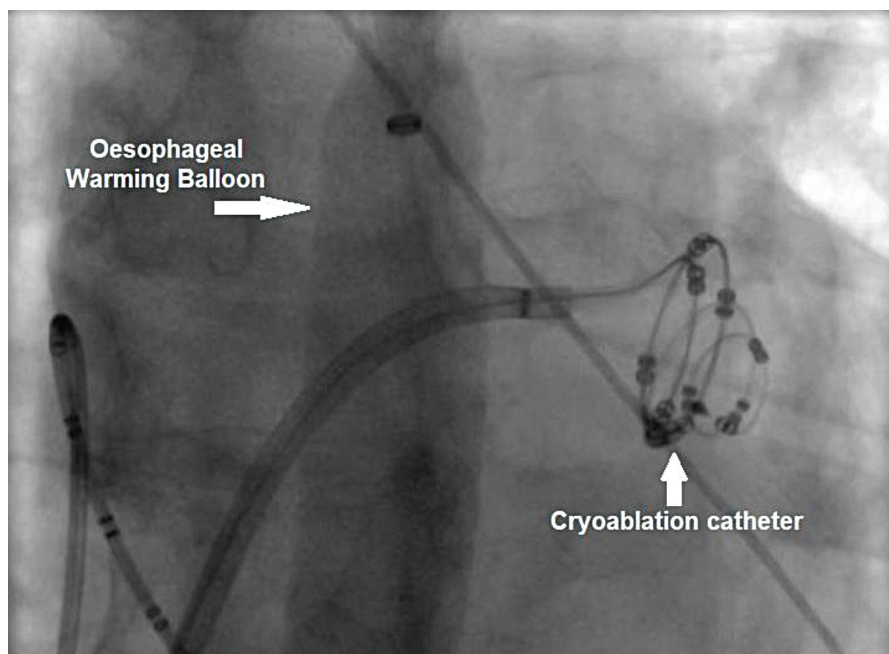
### *The most recent ESC guidelines in 2020 now recognise a rhythm strip diagnosis of >30s to confirm a diagnosis of AF*

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#### **Rate vs rhythm control: No longer equivalent**

Aside from anticoagulation to reduce the risk of stroke, a fundamental principle in the management of AF has been the decision to pursue a rate or rhythm control strategy. Specifically, this means a ventricular rate control strategy, usually with beta-blockers or calcium channel blockers, or a strategy where the goal is to try to achieve and maintain sinus rhythm.

Multiple randomised trials in the early 2000s compared a pharmacological rate control strategy versus a rhythm control strategy with anti-arrhythmic drugs. These trials failed to demonstrate a benefit with the rhythm control strategy.<sup>8,9,10</sup> This



**FIGURE 3:** Fluoroscopic image of the adagio cryoablation catheter conforming to the left inferior pulmonary vein

apparent equivalence of rate versus rhythm control was a clear, simple message that was easily adopted at the time by the wider medical community. Immediate changes were observed in the treatment of AF, with less patients being referred for DC cardioversions, and an increase in AV node ablations and acceptance of life-long AF.<sup>11</sup>

The key message we now know from these trials is that the side-effect profiles, arrhythmic risk, and inefficacy of anti-arrhythmic medications offset the benefits of sinus rhythm.

Advances in the treatment of AF have progressed rapidly in recent years and a rhythm control strategy should now be the initial goal in the majority of our patients. This historical message of equivalence when comparing rate and rhythm control strategies across a broad population with AF is now outdated.

#### **Seeking sinus rhythm**

The restoration of sinus rhythm can dramatically improve symptoms and quality-of-life in patients with AF and improves cardiovascular outcomes.

As such, this strategy received a class IA recommendation in the latest ESC guidelines.<sup>12</sup> Options to achieve sinus rhythm include electrical cardioversion, pharmacological cardioversion, and catheter ablation.

Electrical cardioversion is a well-tolerated, straightforward procedure with acute success rates in excess of 94 per cent.<sup>13</sup> However, other than transient atrial stunning post cardioversion,<sup>14</sup> the atrial conditions that led to the development of AF are unchanged. As a result, recurrence rates of AF can be as high as 80 per cent within a year.<sup>15</sup> Nevertheless, acute cardioversion can be beneficial in restoring sinus rhythm while a long-term approach is being considered, or to ascertain if indeed the patient feels better in sinus rhythm. When long-term maintenance of sinus rhythm is the goal, the next step is to decide whether to proceed with catheter ablation or to commence anti-arrhythmic drug therapy.

#### **Advances in catheter ablation**

Since the first description in 1998,<sup>16</sup> catheter ablation of AF has undergone

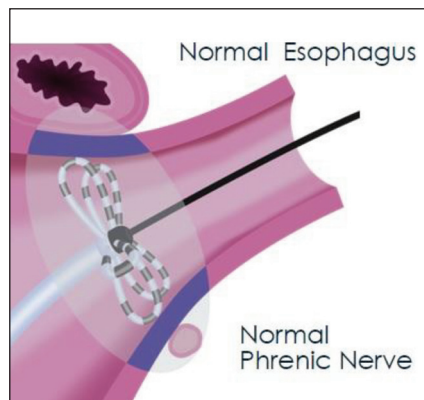
multiple iterative improvements and benefited from technological advancement. The cornerstone of the procedure remains electrical isolation of the pulmonary veins. This target is due to the anatomical discovery that atrial tissue often extends into the pulmonary veins and ectopic beats arising here traverse into the body of the atrium and initiate AF. Currently, the two leading techniques used worldwide are point-by-point radiofrequency ablation (Figure 2) and cryoablation.

Several trials have compared these two techniques, the most notable being the FIRE AND ICE trial,<sup>17</sup> in which over 700 patients with paroxysmal AF were randomised to a strategy of radiofrequency or cryoballoon ablation. Arrhythmia-free survival and complication rates for both techniques were similar, with a shorter overall procedure time using cryoballoon, albeit at the expense of a greater fluoroscopy time.

Both radiofrequency and cryoablation procedures are continually improving. For radiofrequency ablation, randomised trials have demonstrated the use of catheters displaying contact force,<sup>18</sup> steerable sheaths<sup>19</sup> and general anaesthesia<sup>20</sup> all lead to procedural improvements. For cryoablation, newer generations of cryoballoons and improved mapping catheters lead to faster and more effective pulmonary vein isolation, thereby reducing total procedural time and exposure to ionising radiation.<sup>21</sup>

### Procedural time reductions

The progressive reduction in overall AF ablation procedure time is a consistent finding. One of the earliest randomised control trials in radiofrequency ablation in 2005 reported mean procedure times of four hours and 44 minutes.<sup>22</sup> Between 2016 and 2018, the total procedural time in over 3000 ablations performed across 24 US centres was three hours,<sup>23</sup> while in 2020 the multicentre VISTAX study reported times of two hours and 36 minutes with two of the centres reporting times of approximately two hours.<sup>24</sup> Advances in cryoballoon ablation have led to procedure times of



**FIGURE 4:** Image depicting the electrical field selectively targeting atrial tissue with sparing of the esophagus and phrenic nerve. (Reddy VY et al JACC 2019;74(3):315-2)

two hours and 19 minutes in a recent multicentre randomised trial,<sup>25</sup> and as low as one hour and three minutes when safely performed without general anaesthesia.<sup>26</sup> Newer technologies, discussed later, are reporting even shorter times.

### Current waiting list challenges

The goal of restoring sinus rhythm has historically been to improve the quality-of-life (QoL) of a patient with AF. Therefore, when resources are being directed to acute services or prioritised to life-saving interventions, the waiting list for QoL interventions inevitably grows.

The natural history of AF usually begins with brief self-resolving episodes, termed paroxysmal AF. Unless addressed, this will develop into persistent episodes that last longer and may not self-resolve, thereby requiring a cardioversion to restore sinus rhythm. This form of persistent AF is indicative of atrial myocardium with more advanced disease. It is therefore unsurprising that success rates for treatment begin to decline once the AF has reached this stage. Patients will undoubtedly have progression of their illness during their time on a waiting list.

The improvements in ablation technique and reduced procedure times are vital as we try to face the challenges of current waiting lists. Recent data from the National

Treatment Purchase Fund (NTPF) shows over 70,000 patients are awaiting inpatient or day case treatment, with the number in cardiology over 3,300.<sup>27</sup> Efficient use of resources and faster patient throughput will always help, but with ongoing inpatient bed shortages, combined with often insurmountable winter seasonal pressures, further intervention is required.

The utilisation of private hospitals, and the capacity to offer diagnostic and therapeutic interventions, was welcomed throughout the Covid-19 pandemic. As part of the 'safetynet' agreement between the HSE and private hospitals, over the last 24 months many public hospitals, including St James's Hospital, Dublin, and the Mater Misericordiae University Hospital, Dublin, have utilised cardiology capacity at Blackrock Clinic to treat many patients with time-critical cardiac conditions. This has freed up valuable resources, including ICU capacity, at these hospitals to care for patients being admitted through their emergency departments for urgent Covid-19 and non-Covid conditions. Dedicated electrophysiology lab lists offering AF ablations to patients through the NTPF scheme continue to run successfully and reliably. Performed with cardio-thoracic surgical support if required, these lists are less susceptible to the uncertainty of protected lab time and bed availability issues that occur within designated primary percutaneous coronary intervention (PCI) centres that must rightly prioritise unwell acute admissions.

### New technologies

Acute electrical isolation of the pulmonary veins is almost always achievable with current systems and acute success rates continue to improve. A new focus for emerging technologies is durable isolation and improved procedural safety.

A new technology in use in the Blackrock Clinic is the Adagio Medical Cryoablation system (Figure 3). Rather than using the more common cryoballoon technology, the Adagio system uses a circular catheter than can be shaped to

multiple configurations and conform to anatomical variations of the pulmonary veins. An oesophageal balloon circulating warm saline also preserves oesophageal temperature during freezes.

Another exciting area of advancement is the development and use of pulse field ablation (PFA). This non-thermal ablation modality uses ultra rapid electrical pulses to destabilise cell membranes and can selectively ablate myocardial tissue. The expectation is that this modality will reduce procedure-related complications associated with ablation, including phrenic nerve and oesophageal injury (Figure 4).<sup>28</sup>

Published trials have demonstrated that individual pulmonary vein isolation can occur within a matter of seconds and the hope is that PFA will routinely reduce procedural times to one hour or less.<sup>29</sup> PFA technology will be available in Ireland within the next few months, and may become the standard of care if ongoing randomised trials prove the long-term efficacy of the technology provides equivalent or superior arrhythmia-free survival rates.

### A hopeful future

Our understanding of AF continues to evolve and lead to improvements in patient care. A landmark study in 2020 showed that rapid introduction (~36 days from first diagnosis) of a rhythm control strategy to minimise AF reduced stroke and death from cardiovascular causes.<sup>30</sup> Interestingly, 30 per cent of the cohort were asymptomatic.

Opportunistic screening in all patients over the age of 65 is now recommended to detect sub-clinical AF,<sup>12</sup> and the availability of smartphones and handheld screening devices make securing a diagnosis easier than ever.

Earlier diagnosis and referral to specialist services, in conjunction with state-of-the-art technology available to Irish patients, allows us to offer the correct treatment and prevent serious downstream consequences from the growing burden of the world's most common sustained arrhythmia. ■

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