



Taking the pulse on cardiovascular health innovation

Investment opportunities arising from this theme

Executive Summary

- Theme-driven investing involves identifying long-term sources of growth and the companies best positioned to capture the potential profits
- The GIB AM Sustainable World Strategy has a specific Cardiovascular Health sub-theme, focused on investing in companies that are improving access to life-saving treatments and promoting global health equity
- A promising new treatment, Pulsed Field Ablation (PFA), has shown great potential in transforming outcomes of Atrial Fibrillation (AF), an increasingly widespread cardiovascular condition.
- Forecasts suggest that the electrophysiology market will grow to \$11 billion and that PFA's share of the market will expand from just over 5% to 60%-80%¹
- **Boston Scientific (BSX),** a core portfolio holding, produces one of just two FDA approved PFA devices, and is therefore well positioned to take advantage of the increasing adoption of this technology



Medical innovation is a clear example of the Flywheel Effect. History demonstrates that as societies and technology progress, medical challenges frequently evolve alongside them, resulting in further innovation. The Black Death took over four years to spread across Europe, advancing at just a mile a day. Covid-19 spread globally in a matter of weeks, in large part due to the modern worlds' interconnectedness and access to international travel. The resulting vaccine, developed by Pfizer-BioNTech was delivered through innovation in mRNA (messenger RNA) technology.

Medical background of Atrial Fibrillation

Scientific and technological advancement over the last 50 years has lifted millions out of poverty, yet in turn the world's population is increasingly aging and exposed to risk factors resulting from more sedentary lifestyles.



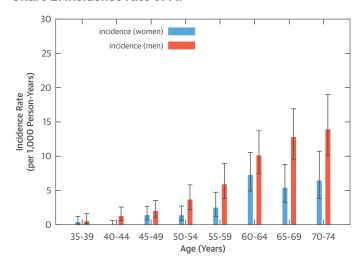






Atrial Fibrillation (AF) offers a prime example of a widespread health concern that has been worsened by society's progression, and ability to live longer. AF is relatively common, with 1 in 45 people in the UK known to be living with the condition.2 Elton John, Miley Cyrus, Tony Blair, and Joe Biden are all well-known individuals who reportedly suffer from the condition. The likelihood of developing this condition is increased by a variety of lifestyle factors including alcohol and tobacco use, physical inactivity, and obesity - risk factors associated with societal advancement. Additionally, as the risk of AF increases with age, it is expected to become even more prevalent in our aging population.3

Chart 1: Incidence rate of AF 4



AF is characterised by a chaotic and irregular heart rhythm, caused by misfiring cells. The condition can lead to a variety of issues ranging from palpitations and dizziness, to stroke and death in more severe cases. In fact, a 2016 study found that having AF raised a person's overall mortality risk by 46%, and a near doubling in their likelihood of stroke.5

AF can be difficult to diagnose early. The condition ultimately requires electrocardiogram (ECG) tracing of the heart to record the abnormal rhythm. However, as many of the symptoms are often vague and easily dismissed (such as dizziness and tiredness), individuals are often only diagnosed once they suffer severe symptoms requiring urgent medical attention. In some cases, wearable devices such as Apple watches (an interesting example of innovative medical technology) can alert individuals to this dangerous heart rhythm before they become symptomatic. However, these devices are not yet widely accepted by medical professionals due to concerns regarding their accuracy.6

Current management of AF initially involves giving medications that help slow down the heart rate and bring it back into a normal rhythm, typically along with blood thinning medications to reduce the risk of stroke. If these medications do not succeed in bringing the heart rhythm under control, a more invasive intervention (called 'ablation') may be required.7

¹ https://investors.bostonscientific.com/-/media/Files/B/Boston-Scientific-IR-V3/2023-BSX-investor-day-slides.pdf

 $^{^2}$ https://www.bhf.org.uk/what-we-do/news-from-the-bhf/news-archive/2023/may/new-figures-show-the-number-of-uk-people-with-heart-rhythm-condition

https://doi.org/10.1016/j.jacc.2015.06.1314

https://doi.org/10.1136/bmj.i4482

Atrial Fibrillation: A Guide to Wearable ECG Smart Watches (afibinstitute.com.au)

Oralle Property of AF | Management | Atrial fibrillation | CKS | NICE



Why Pulsed Field Ablation (PFA) is a promising solution

PFA is a new and promising approach to the treatment of AF. Traditional ablation relies on destroying misfiring heart tissue with thermal energy which is effective but runs the risk of damaging surrounding structures, including nerves and veins.^{8,9,10} In contrast, PFA administers short duration pulses of a high-voltage electrical signal instead of thermal energy. As cells in the heart use electrical energy to function, PFA preferentially targets and destroys heart tissue, therefore reducing the risk of damage to surrounding structures.

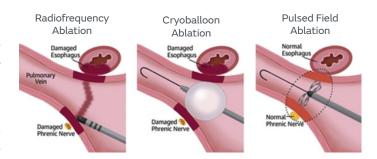
PFA has shown great promise, not only demonstrating high efficacy (with a low 1-year rate of recurrence of AF) but also a more favourable side effect profile than traditional thermal ablation.¹¹ Furthermore, numerous studies have found PFA can be completed in under an hour, which is much faster than the standard 2 hour procedures seen with thermal ablation.¹² These shorter procedure times can offer clinicians the opportunity to improve their patient flow and perform more interventions.

Studies comparing treatments have found that ablation has better efficacy than medications and less recurrence of arrhythmia (abnormal heart rate), without the side effects associated with these drugs. ^{13,14} Given the high efficacy and improved safety profile of PFA, it is therefore not unreasonable to suggest that it has the potential to not only surpass other ablation techniques, but also to replace medical management of AF altogether.

Pulsed Field Ablation System 15



Pulsed Field Ablation for Pulmonary Vein Isolation in Atrial Fibrillation ¹⁶



Exposure of medical device companies to PFA

While several companies manufacture medical devices for electrophysiology (the field in which PFA is categorised), Boston Scientific's "FARAPULSE" system is one of only two PFA systems to have received FDA approval in the US. At the time of writing. FARAPULSE has a wealth of clinical trial data so far to support its safe and effective use.



- ⁸ Catheter Ablation of Atrial Fibrillation: An Overview for Clinicians | Advances in Therapy (springer.com)
- 9 How to Prevent, Detect and Manage Complications Caused by Cryoballoon Ablation of Atrial Fibrillation PMC (nih.gov)
- ¹⁰ Severe Pulmonary Vein Stenosis Resulting From Ablation for Atrial Fibrillation | Circulation (ahajournals.org)
- 11612 Pulsed Field Ablation for the Treatment of Atrial Fibrillation: PULSED AF Pivotal Trial | Circulation (ahajournals.org)
 13 Catheter ablation as first-line treatment for paroxysmal atrial fibrillation: a systematic review and meta-analysis | Heart (bmj.com)
- ¹⁴ Treatment of Atrial Fibrillation With Antiarrhythmic Drugs or Radiofrequency Ablation | Circulation: Arrhythmia and Electrophysiology (ahajournals.org)
- 15. FARAPULSE Pulsed Field Ablation System Boston Scientific
- 16 Reddy, V, Neuzil, P, Koruth, J. et al. Pulsed Field Ablation for Pulmonary Vein Isolation in Atrial Fibrillation. J Am Coll Cardiol. 2019 Jul, 74 (3) 315–326.
- 17 https://www.bostonscientific.com/en-EU/medical-specialties/electrophysiology/

Boston Scientific, a core holding in the GIB AM Sustainable World Strategy, is a company whose medical devices help approximately 30 million patients annually. It prides itself on its drive to innovate, frequently acquiring new devices to add to their range whilst investing significantly in research and development initiatives.

In 2023, cardiovascular devices made up the majority of Boston's revenue (circa 62%), versus electrophysiology which made up c.6% of revenue. However, by 2028, Boston Scientific forecasts that the electrophysiology market will grow to \$11 billion and that PFA's share of the market will expand from just over 5% to 60%-80%.

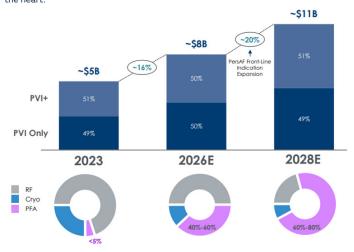
While the use of PFA is still in its infancy, it is expected to grow rapidly in coming years, and we believe that Boston Scientific, with its strong track record of innovation and expertise in cardiovascular devices, is primed to take advantage of this.

Global AF procedures by procedure type 18

\$ Revenue, CAGRs, Procedure Share (%)

PVI: Pulmonary Vein Isolation, ablation that just targets heart tissue in the region of the pulmonary veins.

PVI+: Ablation that targets the pulmonary vein region, in addition to other sites in the heart.



¹⁸ PowerPoint Presentation (bostonscientific.com)

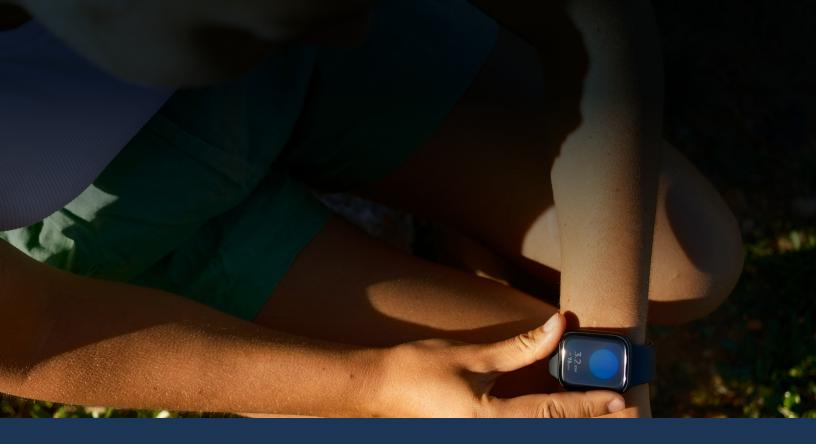
Investment conclusion

In a world increasingly impacted by chronic disease, aging populations, and evolving health risks, Healthcare themes such as Cardiovascular Health are providing more investment opportunities for multi-thematic investors than ever before.

By offering a safer, faster, and more efficient alternative to traditional ablation techniques, PFA represents a significant leap forward in the treatment of the growing AF condition.

While the use of PFA is still in its infancy, it is expected to grow rapidly in coming years. We believe that companies like Boston Scientific, with strong track records of innovation and expertise, are primed to take advantage of these technological advances over the long term.





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