Let there be light! The meteoric rise of cardiac imaging

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ABSTRACT

Imaging plays a central role in modern cardiovascular practice. It is a field characterised by exciting technological advances that have shaped our understanding of pathology and led to major improvements in patient diagnosis and care. The UK has played a key international role in the development of this subspecialty and is the current home to many of the leading global centres in multimodality cardiovascular imaging. In this short review, we will outline some of the key contributions of the British Cardiovascular Society and its members to this rapidly evolving field and look at how this relationship may continue to shape future cardiovascular practice.

INTRODUCTION

When the British Cardiovascular Society (BCS) evolved from the Cardiac Club 100 years ago, the sole method of imaging the heart was X-ray. The field had not progressed greatly by 1939, when the first volume of the British Heart Journal contained a detailed description of how fluoroscopy could be used to estimate cardiac chamber size and shape.¹ While some of our interventional colleagues may still consider this the reference standard, the intervening years have witnessed an explosion in technology with multiple complementary imaging approaches now readily available. Moreover, the excitement of looking our enemy in the eye remains similar to F H Williams' first description back in 1896 of how X-ray might visualise the heart 'through a waistcoat and two shirts'. The sartorial elegance of UK cardiologists may have irreversibly declined since those words, yet our passion and enthusiasm for this important field has flourished. In this review, we will recount the past century's development of cardiovascular imaging and the major contributions that BCS members have made. These are many and varied and have established British cardiology as a major contributor to this important field. This review will also cast an eye to the future providing a contemporary take on the same two questions posed by A L Muir in his Jubilee Editorial in 1987,3 written to mark the 50th anniversary of the BCS. 'In 2037 which of today's [imaging] methods will still be in use?' and 'Will imaging be based on a physical phenomenon yet to be explored?' Insightful queries that remain of major relevance today and which we will also address.

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ECHOCARDIOGRAPHY

In an era of multimodality imaging, echocardiography may be considered a 'traditional modality', however the diverse range and scope of echocardiographic techniques available to the contemporary clinician is staggering, as is its future potential. Echocardiography has, for decades, been the first-line, reference standard imaging technique for most cardiovascular conditions, providing an excellent illustration of how technology has evolved during this time (figure 1). The need for ever clearer images and more granular data has driven rapid scanner development bringing cardiac ultrasound closer to, next to, or even into the heart. Echocardiography is already used to scan patients at their bedside anywhere in the hospital. In future, the newest handheld echocardiographic scanners may soon replace the stethoscope as the iconic symbol of the cardiologist, while smart phone echo probes may go yet further transferring the power of imaging directly into the hands of the patient. Far from an outdated technology, echocardiography may yet prove imaging's most revolutionary modality.

The rate of growth in echocardiography across the UK cannot be underestimated. Within the lifetime of many current cardiologists, echocardiography has grown from being a niche technique, of limited clinical use, to a foundational diagnostic tool in cardiovascular practice, probably second only to the resting ECG⁴ (figure 1). Despite some initial scepticism, 'Reflected ultrasound as a diagnostic instrument in study of mitral valve disease' was published in the British Heart Journal in 1967. In 1969, Dr J P Shillingford, better known as a pioneer of the coronary care unit, held a symposium at the Royal Society of Medicine where the 'avant garde' concept of non-invasive flow velocity measurements with Doppler directional velocimetry was discussed.⁵ By 1974, the BCS had created a 'Working Party on Echocardiography' (the American Society of Echocardiography (ASE) was not founded until 1975), which within a year had petitioned the Department of Health and Social Security for the widespread availability of echocardiography across the National Health Service (NHS). Relatively sizeable and comprehensive echo services were described in UK district general hospitals as early as 1978.6 By 1980, the year that the ASE defined the standard echocardiographic views in use today, echocardiography was described by the Royal College of Physicians of London and the Royal College of Surgeons of England as an essential skill required by all cardiac 'technicians' working in cardiac centres, and 'highly desirable' in subspecialty cardiology consultants. Open access to echo in primary care was commonplace by the late 1990s.

In terms of research, the 'cutting-edge' echocardiography first presented to the BCS annual





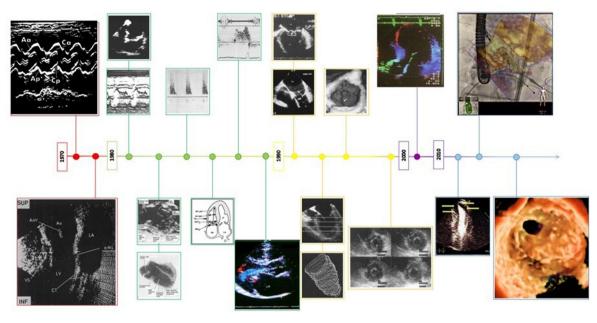


Figure 1 A timeline of progress in echocardiography. Left to right (all images are from British institutions, or published in British Journals). 1974: first demonstration of the clinical utility of echocardiography in aortic valve disease. 1977: a demonstration of two-dimensional echocardiography with a wide angle (600) sector scanner. 1982: myxomatous degeneration of mitral valve. Typical M-mode findings are shown, with mitral valve thickening and prolapse in the four-chamber view. 1984: echocardiographic and anatomical correlations in fetal congenital heart disease. Ebstein's anomaly is shown. 1985: early continuous wave Doppler echocardiography in the assessment of adults with aortic stenosis. 14 1986: a systematic approach to the evaluation of the right ventricle, still in use today. 1988: patterns of diastolic dysfunction in left ventricular hypertrophy. 1989: early demonstration of the use of colour flow Doppler in aortic regurgitation. 1994: practical description of how to set up a transoesophageal echocardiography service. 1995: early utility of three-dimensional echocardiography for left ventricular assessment. 1995: early utility of three-dimensional echocardiography for aortic valve assessment. 1997: stress echocardiography in the assessment of left ventricular ischaemia and viability. 16 2010: tissue Doppler echocardiography. 2014: perfusion echocardiography demonstrating an apical perfusion defect. 24 2016: fusion echocardiography-flouroscopy to facilitate contrast-free transcatheter aortic valve implantation. 27 2018: 'TrueVue' three-dimensional echocardiography demonstrating mitral valve perforation. 28 Aa and Ap, anterior and posterior aortic root walls; aML, anterior mitral leaflet; Ao, aortic root; AoV, aortic valve cusps; aRV, anterior right ventricular wall; Ca and Cp, echoes from the anteriorly and posteriorly positioned aortic valve cusps; CT, chordae tendineae; Inf. inferior; LA, left atrium; LV, left ventricle; PM, papillary muscle; Sup, superior; VS, ventricular septum.

scientific meeting in 1967 would be almost unrecognisable today. Around the same time the British Journal of Radiology described the utility of M-mode 'ultrasound cardiography' in patients with mitral and some forms of tricuspid valve disease. as well as occasionally in those with aortic valve disease, atrial myxomas and pericardial effusions.9 The 1980s heralded an explosion of research in echocardiography (figure 2). As the quality of 'cross-sectional two-dimensional (2D) echocardiography' improved from vague shades of grey to something more closely resembling today's moving images, British cardiology produced seminal works in establishing normal reference values and then studies in valvular heart disease, 10 stress echocardiography, 11 fetal and paediatric echocardiography, 12 13 as well as pulsed wave, continuous wave, and colour Doppler. 10 14 The early 1990s saw a boom in three research areas, subsequently adopted into routine clinical practice: transoesophageal echocardiography (TOE), 15 stress echocardiography and the quantification of ventricular function. ¹⁶ ¹⁷ The 21st century advances include three-dimensional (3D) echocardiography, 18-21 strain imaging and tissue Doppler.²² These now 'basic' technologies remain the cornerstone of assessing anatomical, functional and pathophysiological effects of cardiovascular disease, with further recent UK research advances in contrast echocardiography^{23–25} and the application of 3D printing²⁶ and artificial intelligence.²⁷

Finally, the role of echocardiography in the development of new treatment options for structural heart diseases has grown

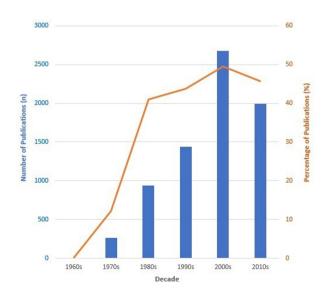


Figure 2 The growth of echocardiographic research and publication in the British Heart Journal/Heart. The blue bars represent the absolute numbers of publications in the British Heart Journal/Heart since the first mention in 1967. The orange line represents these absolute numbers as a percentage of total publications for that decade.

dramatically over the past decade, with novel catheter-based approaches such as transcatheter aortic valve implantation (TAVI), MitraClip, transcatheter mitral valve replacement, left atrial appendage occlusion and atrial septal defects closure.²⁸ Multimodality imaging has played a crucial role in the success of these procedures, introducing routine echocardiography into the catheter lab. The development of intracardiac echocardiography has applications in electrophysiology and structural interventions. Single-use percutaneous transvenous 2D, 3D and four-dimensional (4D) probes²⁹⁻³¹ are available with the major advantage over TOE being the ability to image the heart without the need for general anaesthesia. These advances, while important for patients, have also heralded the dawn of a brand-new subspecialty: the interventional imager. A new generation of highly skilled, multimodality imagers that lie at the centre of the heart team, coordinating pre-procedural planning, intraprocedural guidance and post-procedural follow-up for all the many new interventional procedures being developed.

NUCLEAR CARDIOLOGY

Nuclear imaging of the cardiovascular system using single photon emission CT (SPECT) and positron emission tomography (PET) is widely used to assess patients with cardiovascular disease, traditionally for the investigation of myocardial perfusion, where the passage of radiotracers into the myocardium can be imaged and quantified (PET) during rest and stress. Important contributions to this field have been made by British investigators; Royal Brompton & Harefield Hospitals investigating the effect of a range of different exercise and pharmacological stress agents ^{32–34}; Cambridge University demonstrating the cost-effectiveness of nuclear perfusion imaging techniques ³⁵; and the Hammersmith Hospital investigating PET myocardial perfusion, its relationship with coronary artery stenosis and its global reduction in patients post-myocardial infarction. ³⁶ ³⁷

More recently, SPECT and PET imaging have been used as tools for molecular imaging, allowing investigation of myocyte function and disease activity to complement the structural information provided by other imaging approaches. ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG) PET has been used for many years as the reference standard assessment of myocardial viability imaging. However, ¹⁸F-FDG is also used clinically as a marker cardiovascular inflammation, recently adopted into clinical guidelines for the assessment of cardiac infection ³⁸ ³⁹ and cardiac

sarcoidosis.⁴⁰ ⁴¹ Additionally, bone scintigraphy techniques are now widely used in the diagnosis of transthyretin cardiac amyloidosis using techniques (eg, ^{99m}Tc-pyrophosphate, ^{99m}Tc-3,3-diphosphono-1,2-propanodicarboxylic acid) on the basis of work from British investigators.⁴²

Exciting recent developments now allow cardiovascular disease activity to be measured using a range of different tracers that can investigate inflammation (¹⁸F-FDG, 68Ga-Dotatate), ⁴³ ⁴⁴ calcification activity (¹⁸F-sodium fluoride), ⁴⁵ thrombus formation (¹⁸F-GP1) and sympathetic innervation (¹²³I-metaiodobenzylguanidine). ⁴⁷ Coupled with advanced motion correction techniques and post-processing software, the UK is leading this exciting new era of molecular cardiovascular imaging that has been applied to a wide range of cardiovascular conditions including atherosclerosis (figure 3), aortic stenosis, aortic aneurysm disease, erectile dysfunction and vasculitis, among others. With the widespread clinical application of similar techniques for patients with cancer and the resulting national infrastructure developments, molecular imaging using nuclear techniques has an exciting future.

COMPUTED TOMOGRAPHY

CT provides highly detailed images and unrivalled anatomical detail, particularly useful in the coronary arteries and the heart valves. CT was invented by the British electrical engineer Sir Godfrey Hounsfield, working at the time for Electrical and Medical Industries. This is the basis for the unlikely link between CT and the Beatles, whose great international success at least in part funded Sir Godfrey's pioneering research. The first patient underwent CT imaging of their brain in October 1971 at Atkinson Morley's Hospital in South London with Sir Godfrey later receiving the Nobel prize in 1979. However, the complexities of cardiac motion ensured that diagnostic CT images of the heart were delayed by several decades and only readily available in the past 15 years (figure 3). Nevertheless, in that short time, CT imaging has assumed a central role in the assessment of cardiovascular patients across the world.

Non-contrast CT imaging of the heart allows quantification of the calcium burden in the coronary arteries: coronary calcium scoring. This serves as a surrogate marker of the overall coronary atherosclerotic plaque burden, providing powerful prognostic information in asymptomatic primary prevention populations. More recently, CT calcium scoring of the aortic

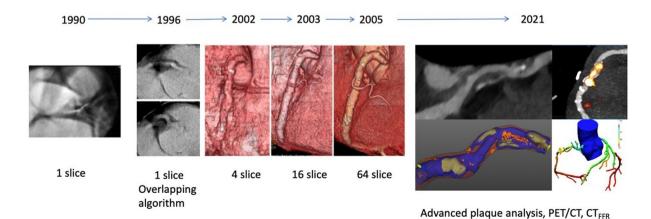


Figure 3 A timeline of progress in cardiac CT. Initial attempts to image the coronary arteries were limited by motion and spatial resolution; however, with the development of 64-slice scanners, robust high-quality imaging of the coronary arteries became a reality. Modern CT images can now provide detailed plaque characterisation and quantification as well as non-invasive assessments of the fractional flow reserve. Hybrid PET/CT scanners allow fusion of PET assessments of disease activity with the anatomical information provided by CT. PET, positron emission tomography.

valve is used as an alternative anatomical assessment of aortic stenosis severity.⁴⁹

Contrast-enhanced coronary CT angiography (CCTA) provides detailed assessment of the coronary lumen as well as atherosclerotic plaque with the ability to accurately define the severity of luminal stenosis and characterise plaque type and burden. This allows detailed assessment of patients presenting to outpatient chest pain clinics and the ability to characterise patients into those with normal coronary arteries (no plaque), non-obstructive plaque, obstructive plaque and three vessel or left main stem disease, helping to direct both the application of secondary prevention medication and the need for invasive angiography and possible revascularisation. The UK-based SCOTHEART randomised controlled trial demonstrated that addition of CCTA to standard care reduced the risk of death from coronary heart disease or non-fatal myocardial infarction in patients presenting with chest pain by 41%. 50 This has led to the widespread clinical adoption of CCTA as a first-line imaging technique for assessing patients with stable chest pain in both national and international guidelines. In patients with aortic stenosis, contrast-enhanced CT is also widely used in procedural planning prior to TAVI, being used to select the preferred access route and for accurate valve sizing (figure 3).⁵¹ Similar approaches are being adopted to guide the transcutaneous treatment of mitral and tricuspid valve lesions.

Recent exciting advances led by UK researchers include detailed assessments of coronary plaque morphology and burden⁵² assessments of coronary plaque inflammation based on changes in the surrounding pericoronary fat⁵³ and the noninvasive assessment of fractional flow reserve, all set to make major contributions to clinical care and risk stratification. The SALTIRE-2 randomised controlled trial will investigate the clinical utility of CCTA in guiding primary prevention therapies in comparison with cardiovascular risk scores.

CARDIOVASCULAR MAGNETIC RESONANCE

In 2003, British physicist, Peter Mansfield, was awarded the Nobel Prize for Physiology or Medicine, based on his 1970s work developing MRI. Like CT, application of this technology to the heart was delayed. However, major progress has been made over the past 20 years, and now cardiovascular magnetic resonance (CMR) is used as a routine clinical imaging tool particularly for the assessment of myocardial disease.⁵⁴ Many of the major developments in CMR that have shaped current practice have been British. These include the development of detailed cine imaging, providing reference standard assessments of left ventricular structure and function.⁵⁵ One of the greatest UK contributions has been stress perfusion CMR. This includes much of the early pioneering perfusion pulse sequences and three large, randomised trials that demonstrated the clinical utility of CMR perfusion and led to its class 1 recommendation in the latest international guidelines. Other notable advances include quantification of valve regurgitation, ⁵⁶ MR spectroscopy ⁵⁷ and myocardial perfusion assessments, ⁵⁸ all driven by key British contributions, widely adopted in clinical practice and all now included in international guidelines.

Another key advantage of CMR is its myocardial soft tissue characterisation. The contrast agent gadolinium accumulates and demonstrates delayed washout in regions of extracellular expansion and scarring. Late gadolinium enhancement imaging therefore provides the unique ability to image replacement myocardial fibrosis across a range of different cardiovascular conditions. The pattern of late enhancement can help differentiate different

underlying conditions (eg, ischaemic vs non-ischaemic cardiomyopathies) but also provides powerful prognostic information across a range of different conditions including hypertrophic cardiomyopathy, ⁵⁹ dilated cardiomyopathy, ⁶⁰ aortic stenosis ⁶¹ and arrhythmogenic right ventricular cardiomyopathy ⁶² to name a few. Ongoing UK-based randomised controlled trials are investigating whether management decisions based on CMR scar imaging improves patient outcomes. ⁶³

Parametric mapping techniques have developed this capability further, with British investigators again leading the way.⁶⁴ T1 mapping, with native T1 and extracellular volume (ECV), inform about diffuse rather than established focal myocardial fibrosis and provide important prognostic information.⁶⁵ Both techniques can be used in the diagnosis of amyloidosis and Fabry's disease. 66 67 T2 mapping informs about myocardial inflammation, while T2* can detect myocardial iron loading. The latter has transformed the monitoring and care of patients with haemochromatosis and those receiving regular blood transfusions and leading to major improvements in patient cardiovascular outcomes.⁶⁸ Recent additional advances include 4D flow, ⁶⁹ myocardial tractography, manganese CMR, rapid CMR protocols, ^{70–72} studies demonstrating the safety of CMR imaging in patients with cardiac devices⁷⁰ and CMR imaging in patients with COVID-19⁷³ all led by UK investigators and set to further develop the role of CMR in clinical practice.

STANDARDS IN BRITISH CARDIAC IMAGING

The primary aim of the BCS is to support and represent all those working in cardiovascular care and research, providing the benchmark for standards of practice. Arguably, one of the great strengths of UK cardiology is its ability to collaborate and evolve alongside different specialties and healthcare disciplines, evidenced by the affiliation of the BCS with numerous national bodies.

Dedicated cardiac physiologists, who are highly trained to undertake and independently report most echocardiograms performed across the country, are a huge and unique asset. The British Society of Echocardiography (BSE), created in 1990, is the largest of the professional groups affiliated to the BCS and facilitates a true collaboration between medical and scientific professional groups, with subsequent recognition of the role of a registered clinical scientist.

The rapid and ongoing evolution of echocardiography, coupled with its diverse clinical scope, provides both opportunity and challenge. The widespread availability of hardware that places echo quite literally in the palm of the examiner's hand demands definable quality standards and is a major stimulus for education and certification. BSE has had a formal accreditation process for transthoracic echocardiography since 1994,⁷⁴ and was the first national organisation to establish a departmental quality standards framework to support individual echocardiographers.⁷⁵ UK cardiologists also contributed to the development of international standards in echocardiography accreditation.⁷⁶ Dedicated training and certification are now available in the UK for the wide scope of echocardiographic practice: level 1 (bedside) transthoracic, transoesophageal, congenital heart disease, critical care and stress echocardiography, the latter reported to be the world's first such programme.

The oldest independent imaging society in the UK is the British Nuclear Cardiology Society founded in 1981, with a focus on promoting, improving and supporting the practice of UK nuclear cardiology, in part through its affiliation with the BCS. Indeed, specific training in echocardiography and nuclear medicine was

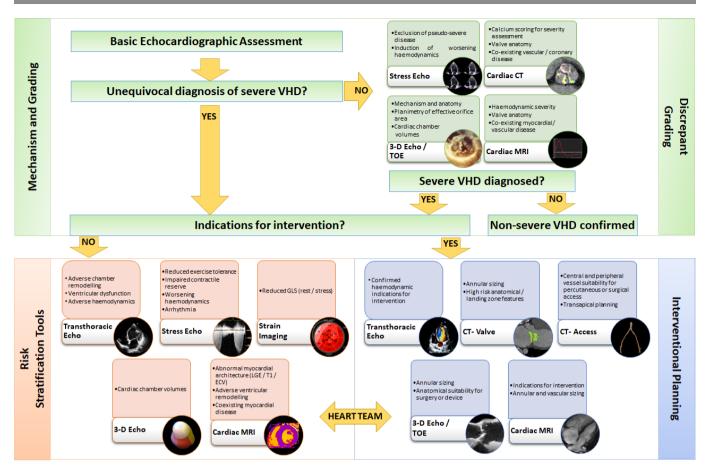


Figure 4 Multimodality imaging, using aortic stenosis as the exemplar. 3-D echo, three-dimensional; echocardiography; CT, computed tomography; TOE, transoesophageal echocardiography, GLS, global longitudinal strain; LGE, late gadolinium enchancement; ECV, extracellular volume, MRI, magnetic resonance imaging.

cited in the guidelines for adult cardiovascular disease training as early as 1985. 77

The British Society of Cardiovascular Magnetic Resonance (BSCMR) was founded in 2006 and has rapidly evolved into the UK's national representative body for CMR. The BSCMR is one of only a few national bodies worldwide dedicated to CMR and represents one of the largest groups of CMR specialists internationally. BSCMR provides guidance on departmental infrastructure, training requirements and governance frameworks that are appropriate for performing clinical CMR in the UK, as well as coordinating multicentre research collaboratives. 61

The British Society of Cardiovascular CT acts as the national specialty group for CT in the UK and forms part of the British Society of Cardiovascular Imaging (BSCI), a multimodality imaging association that is open to cardiologists, radiologists, non-medical specialists and generalists. Both the BSCI and BSCMR provide strict training guidelines and accreditation programmes to promote the highest standards of practice of UK cardiovascular imaging.

MULTIMODALITY IMAGING

With the routine clinical use of an array of different imaging modalities each providing complementary information, the concept of multimodality imaging has emerged. This can be simply defined as using the best imaging technique to answer the clinical question at hand (figure 4). UK investigators have led the way in defining this concept⁷⁸ and in developing training programmes that allow cardiologist to train across multiple

different imaging modalities so that they are best placed to choose the optimal technique for their patients. The BCS UK Imaging Council, incorporating the four modality-specialist societies, encourages this concept by facilitating closer working between the societies, in particular around education and clinical standards.⁷⁹

CONCLUSION

The UK has played a central role in the history and development of cardiovascular imaging. To update A L Muir, not only do we currently use most of the technologies available in 1987, but they remain the foundation of our clinical practice. Yet, we also have a range of novel approaches that together have improved patient diagnosis, risk stratification and therapeutic planning. We therefore stand at the start of a new era of advanced multimodality imaging with the potential to transform the way we practise cardiology if we can use this exciting technology both judiciously and efficiently. In that context, we found it hard to improve on A L Muir's closing remarks from his article over 30 years ago: 'today we must learn to use the available imaging techniques wisely. Tomorrow, we shall have to assimilate the best of the newer methods and discard the others. It would be foolish to predict the state of imaging in 2037.'

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