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## The marvel of percutaneous cardiovascular devices in the elderly

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Thanks to minimally invasive procedures, frail and elderly patients can also benefit from innovative technologies. More than 14 million implanted pacemakers deliver impulses to the heart muscle to regulate the heart rate (treating bradycardias and blocks). The first human implantation of defibrillators was performed in early 2000. The defibrillator detects cardiac arrhythmias and corrects them by delivering electric shocks. The ongoing development of minimally invasive technologies has also broadened the scope of treatment for elderly patients with vascular stenosis and aneurysmal disease as well as other complex vascular pathologies. The nonsurgical cardiac valve replacement represents one of the most recent and exciting developments, demonstrating the feasibility of replacing a heart valve by way of placement through an intra-arterial or trans-ventricular sheath. Percutaneous devices are particularly well suited for the elderly as the surgical risks of minimally invasive surgery are considerably less as compared to open surgery, leading to a shorter hospital stay, a faster recovery, and improved quality of life.

**Keywords:** pacemakers; defibrillators; stents; stent-grafts; percutaneous heart valve; elderly; high risk patient

### Introduction

Blood supply to the whole body cannot be impaired unless dramatic consequences follow, including lethal issues. Peter Schneider's statement: "I am a believer in good blood supply" might be every cardiovascular physician's motto.<sup>1</sup> Globally an aging population requires increasing healthcare services. Minimally invasive procedures and implants allow many patients to now be offered a therapeutic option that until recently did not exist, thus permitting their survival and/or enhanced quality of life. A myriad of implants have been developed which can ameliorate problems in cardiovascular surgery (valves, stents, stent-grafts, and vascular prostheses), physiologic or endocrine support (blood oxygenators, artificial kidneys, artificial livers, artificial pancreas), structural or functional support (orthopaedic implants, ophthalmic implants) and transmission of electrical or sensory signals (pacemakers and defibrillators, cochlear implants, and visual implants).

Elderly and frail patients who have certain types of dysarrhythmias can now benefit from signal transmitting devices, which guarantee the mechanical function of the heart. More than 15 million pacemakers, which deliver impulses to the heart muscle to regulate the heart rate (bradycardia and block), have been implanted. This technology has evolved rapidly since the first human implantation by Ake Senning in 1958.<sup>2</sup> The first human implantation of defibrillators capable of delivering higher energy electrical pulses to treat ventricular fibrillation and tachycardia were performed at the turn of the century.<sup>3</sup>

Other pathologies which are now being treated in this minimally invasive manner include arterial stenosis and aneurysms. Dotter, Grüntzig, and Palmaz pioneered angioplasty and stenting of arteries to nonsurgically dilate stenotic or calcified vessels since the early 1960s.<sup>4-6</sup> Puel was the first to deploy coronary artery stents in humans in 1993.<sup>7</sup> These devices, as well as the newer drug-eluting

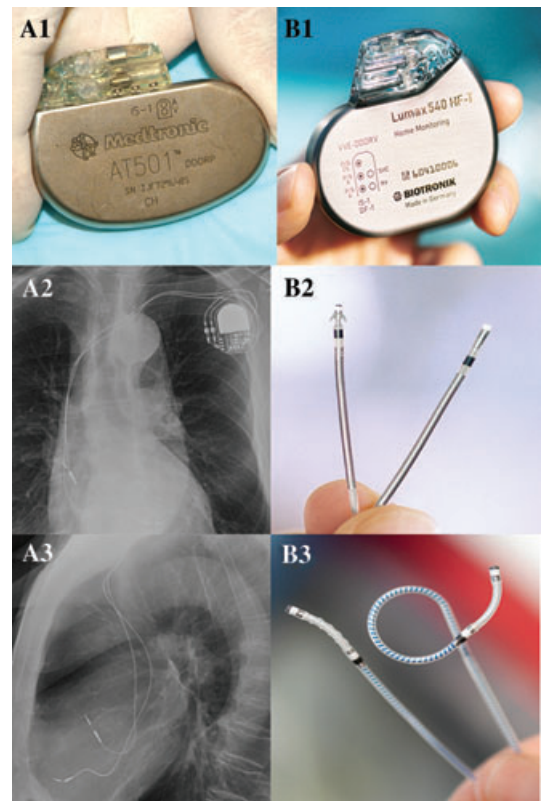
stents, efficiently reverse coronary artery blockage while carotid stents and those deployed in visceral and peripheral arteries, although seemingly effective, require additional validation. Abdominal aortic stent-grafts, based upon the initial concepts developed by Kononov (1979),<sup>8</sup> Parodi (1989),<sup>9</sup> and Mialhe (1993),<sup>10</sup> treat abdominal aortic aneurysms by excluding the aneurysm by manner of exclusion from within the vessel. This technology is maturing rapidly and has become the preferred therapy for the treatment for the thoracic aneurysms and dissections. The nonsurgical implantation of an aortic valve by Cribier in 2001 represents a landmark in the treatment of aortic valvular dysfunction in the elderly.<sup>11</sup> It has been demonstrated that it is feasible to replace a failed aortic heart valve by passing a stent-mounted valve through a catheter from the patient's groin. This is particularly important as more than 20% of the candidates for a valve replacement are  $\geq 80$  years old. It is becoming evident that percutaneous devices are particularly well fitted for the elderly as the risks of minimally invasive surgery are considerably less as compared to open surgery leading to shorter hospital stay and faster recovery. These new minimally invasive cardiovascular treatment options have led to an overall improved quality of life for many older frail patients who would have previously been refused surgical therapy.

### Signal transmitting devices

Each individual heartbeat results from the electrical impulses originating from the sinoatrial node, that is, the natural pacemaker. This node, comprised of electrically active cells located in the upper right chamber, sends a steady stream of electrical signals along a pathway through the heart's upper chambers. These signals then travel to the atrioventricular bridge between the upper and lower chambers and finally terminate in the lower chambers. The cardiac electrical system sets the heart rate and coordinates the contraction of the heart muscle so that the heart beats efficiently. Abnormalities of the cardiac electrical system are manifested by cardiac arrhythmia: bradycardias (abnormally slow) or tachycardias (abnormally rapid) (Fig. 1).<sup>12</sup>

### The pacemakers

These devices analyze the function of the heart's own electrical system and, when necessary, send precisely



**Figure 1.** Pacemaker Medtronic AT501. It is a double chamber device fitted with two electrodes and rate responsive (A1, A2, A3). And Biotronik Lumax 540 ICD incorporating technology for wireless remote monitoring of the patient (B1) and defibrillator leads to carry the electrical signal from the device to the heart and information about the heart's natural activity back to the device. The Biotronik Linux SD features active fixation and steroid eluting (B2). The Biotronik Corox OT lead is polyurethane coated and features a helically preshaped distal end and an electrically active electrode coated with iridium (B3). (Courtesy of Biotronik.)

timed electrical signals to initiate a heart beat. The pacemaker is like a pulse analyzer and generator and it will activate itself when there is no heart activity after a preset period of time. It therefore helps to regulate the heart rate to a predetermined level. The pacemaker effectively eliminates the symptoms associated with bradycardia, that is, weakness, fatigue, dizziness, and loss of consciousness.

Pacemakers consist of two major parts: the generator, a tiny hermetically sealed computer that regulates the rate of electrical pulses sent to the heart.

This sealed computer together with the electrical circuitry and the battery are housed in a titanium container. The battery life of most pacemakers today is, on average, 5–8 years. The lead is a flexible insulated wire in which one end is attached to the generator and the other end is passed through the vein into a chamber of the heart. Frequently, two leads are placed, one in the right atrium and the other in the right ventricle. The pacemaker leads transmit the electrical activity of the heart to the pacemaker circuitry. After analyzing this activity, it decides whether to pace. A tiny electrical signal is transmitted to the heart if the heart rate becomes too slow, thus stimulating the heart muscle to contract. Pacemakers that have 2 leads can also maintain the optimal coordination between the atria and the ventricles by pacing the atrium and the ventricle in sequence. In addition to traditional pacemakers, biventricular pacemakers can be used as a treatment option for patients whose hearts' electrical systems have been damaged. Unlike a regular pacemaker, a biventricular pacemaker stimulates both the lower chambers of the heart (the right and left ventricles) to make the heart beat more efficiently. A biventricular pacemaker paces both ventricles so that all or most of the ventricular muscle pump together. The heart in this way pumps blood more efficiently. This is referred to as cardiac resynchronization therapy (CRT).

The clinical indications for pacemaker implantation have been formulated in the standard ACC/AHA format and have been published based upon consensus of task forces from the American College of Cardiology and the American Heart Association.<sup>13</sup> The various options include: single versus dual chamber devices, unipolar versus bipolar configuration, presence of rate, and type of sensor use.<sup>14</sup> Rate-responsive pacemakers are also available. The programming of the pacemakers can be individualized for each patient's needs and can be changed without surgical intervention with an external programmer. The leads connecting the pacemaker to the heart chambers are available with different characteristics but the most important is active versus passive fixation mechanisms. Figure 1B and C are an example of two leads, one in the right atrium and the other in the right ventricle, to maintain the normal sequential contraction of the heart starting with the atrium followed by the ventricles.

Patients more than 70 years of age account for greater than 70% of pacemakers implanted. Indications for implantation of pacemakers in the elderly are generally based on symptoms, the presence of diseases, and the presence of symptomatic bradyarrhythmias.<sup>15–18</sup>

### Implantable cardioverter-defibrillation (ICD)

They have the capacity to detect cardiac arrhythmias and correct them by delivering sharp electric shocks when the heart rhythm becomes abnormal enough to be lethal. Defibrillation is a technique in which electric signals are given in order to restart the normal heart beat. They are therefore implanted in patients who are at risk of sudden cardiac death due to ventricular fibrillation. The cardiac arrhythmias are corrected with a jolt of electricity. In current variants, the ability to revert ventricular fibrillation has been extended to include both atrial and ventricular arrhythmias as well as the ability to perform biventricular pacing in patients with congestive heart failure (CHF). They are permanent safeguards against sudden lethal abnormalities. ICDs constantly monitor the rate and rhythm of the heart and can deliver a jolt when the electrical manifestation of the heart activity exceeds the preset number. Many modern ICDs use a combination of various methods to distinguish between ventricular fibrillation and ventricular tachycardia (VT) and may try to pace the heart faster than its intrinsic rate in the case of ventricular–ventricular (VV) interval measurements, to try to break the tachycardia before it progresses to ventricular fibrillation. This is known as anti-tachycardia pacing. Many modern ICDs use a combination of various methods to determine if a fast rhythm is normal, VT, or ventricular fibrillation by rate discrimination, rhythm discrimination, and morphology discrimination.

The ICDs consist of three main parts: the defibrillator, the leads, and a programmer. The first two parts of the system are implanted in the body.

- The defibrillator is a small metal case that contains electronics and a battery. Similar to the pacemaker it is designed to correct arrhythmia. However, while a pacemaker increases a slow rate, a defibrillator detects and corrects fast and slow heart rates. It must be replaced when batteries are depleted.

- Leads are insulated wires attached to the defibrillator and connected to the heart. They are used both to sense when the heart is experiencing a rhythm that requires a shock and to deliver the therapy. A lead may be inserted through a vein and placed inside the heart (endocardial lead) or attached to the outside of the heart (epicardial lead). One or more leads are used depending on the patient's condition. The leads are left in place unless infections require them to be removed.
- The programmer is a computer used to monitor and adjust pacemakers or implantable defibrillators. It receives information from the device and sends instructions to the device.

ICDs are most commonly implanted in patients who have survived an episode of VT or fibrillation or for a patient whose history suggests a likely hood of developing sustained tachycardia or fibrillation. ICDs have proved to be superior to drugs in prolonging the life of these patients.<sup>19–20</sup> The recommendations for implantation are severe heart arrhythmia in the following cases.

- Patients who have survived a severe cardiac arrest in the past.
- Patients suffering from ventricular fibrillation or VT.
- Patients with dilated cardiomyopathy or hypertrophic cardiomyopathy.

The real value of ICD in elderly patients is questioned by Healey and colleagues.<sup>21</sup> The extrapolation of results from younger patients is likely to overestimate ICD benefit in the elderly.<sup>22</sup> Buxton and colleagues from the MTA Program in UK,<sup>23</sup> have suggested that there is strong evidence based upon randomized control trials suggesting the benefits of ICDs over medical management for ventricular arrhythmias following survival of cardiac arrest in preventing sudden cardiac death in patients at high risks. In patients with NYHA class II or III with CHF and left ventricular ejection fraction (LVEF) of 35% or less, amiodarone has no favorable effect on survival, whereas single-lead shock only ICD therapy reduces overall mortality by 23%.<sup>24</sup> Effective primary prevention of sudden cardiac death with implantable cardioverter was well demonstrated in patients with coronary disease and depressed ventricular function. Elderly patients should be consid-

ered candidates for ICD implantation if life threatening ventricular tachyarrhythmias is present.<sup>24</sup> Goldenberg and Lampert highlighted the evolving indications as well as the numerous advances in ICD technology with emphasis on primary and secondary prophylaxis of sudden cardiac death.<sup>25</sup> Based upon a literature search using the Pulmed and MEDLINE data base, they conclude that cardiac resynchronization improves symptoms, quality of life, and survival for patients with advanced heart failure and intraventricular conductive delays and ventricular dysynchrony. More than 40% of devices are implanted in patients >70 years old and 10% >80-year old. Noncardiac deaths occurred more frequently in older patients but cardiac death rates were similar.<sup>26</sup> Precise criteria for implantation are being discussed between task forces of the American College of Cardiology and the American Heart Association to propose a consensus.

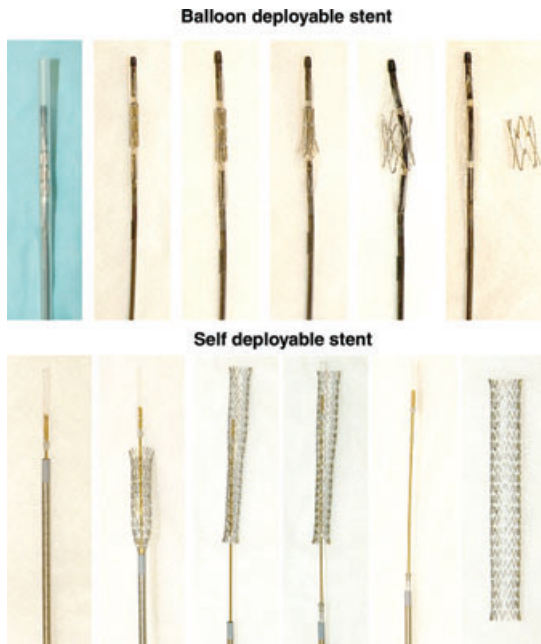
### Blood supply prostheses

They can be used to improve blood supply to the various tissues and the terminal organs in the body by elimination of stenosis and recanalization of normal blood flow together with the prevention of arterial wall ruptures. They can also be used for and replacement of the defective cardiac valves. These implants are now typically deployed percutaneously.

### Stents

In the 1960s, physicians relied on coronary artery bypass graft (CABG) to treat coronary artery disease.<sup>27</sup> The patient's vein or arteries were and are still used to bypass occluded coronary arteries and restore the blood supply to the heart. Dotter, a vascular radiologist introduced transluminal angioplasty in 1964 using multiple dilators.<sup>28</sup> Grüntzig proposed the percutaneous transluminal coronary angioplasty (PTCA) or balloon angioplasty in the 1970s to treat blocked coronary vessels.<sup>5</sup> The patients had quicker recovery times but the initial restenosis rate was as high as 40% within 6 months.<sup>28</sup> However, PTCA continued to be widely accepted throughout the 1980 because it was much less invasive.<sup>29</sup>

Palmaz and Schatz pioneered the concept of a bare metal stent to treat the problem of restenosis.<sup>30</sup> The first stent was a slotted tube of stainless steel mounted on a balloon that could be dilated



**Figure 2.** Pre-mounted 316 L balloon-deployable stainless steel stent 6 mm diameter and 10 mm long and pre-mounted Nitinol stent self-deployable at 5 mm diameter and 40 cm long.

inside the coronary artery. The first coronary deployment in human was done by Puel and Sigwart in 1993.<sup>7</sup> Over the following decades, several generations of bare metal stents were developed based upon strength and flexibility together with easier delivery systems (Fig. 2).<sup>31</sup> The persistent problem of restenosis hindered the bare stent concept. Compared to angioplasty alone, acute artery occlusions were eliminated and the restenosis rate was lower but remained typically about 25% at 6 months. According to Grüntzig, the formation of stenosis is not recurrence of coronary artery disease, but the body's response to the controlled injury of angioplasty characterized by proliferation of smooth muscle cells, roughly analogous to a scar forming over an injury.<sup>32</sup> Concomitant use of clopidogrel an antiplatelet medication has lowered the restenosis rate to less than 10%.

During the 1990s, physicians and companies moved away from the purely mechanical devices toward pharmacological composites. A variety of drugs were selected to interrupt the biological processes that caused restenosis. Stents were either coated with these drugs, sometimes embedded in

a thin polymer for sustained release. The drug eluting stents were able to reduce restenosis from the 25 to 30% range to single digits.<sup>33</sup> However, the patient must take aspirin, clopidogrel (Plavix) or ticlopidine (Ticlid) for a year or more after deployment.<sup>34</sup>

Many of the new generation of stents are partially or completely bioresorbable, but their capacity to impact the market are still limited.<sup>35</sup> A bioresorbable polymer elutes anti-restenosis drug. The polymer coated and/or eluting stents become a bare metal stent after a few months. The completely bioresorbable metallic stents which will totally disappear after it has done its work did not lead to clear cut improvements over previous stents.<sup>36</sup> Currently, a bio-engineered coating to attract a thin endothelial layer shortly after implantation which is likely to promote the healing and thus improve the blood compatibility of the conduit is currently under development.

#### Aortic stent-grafts and covered stents used to treat other peripheral pathologies

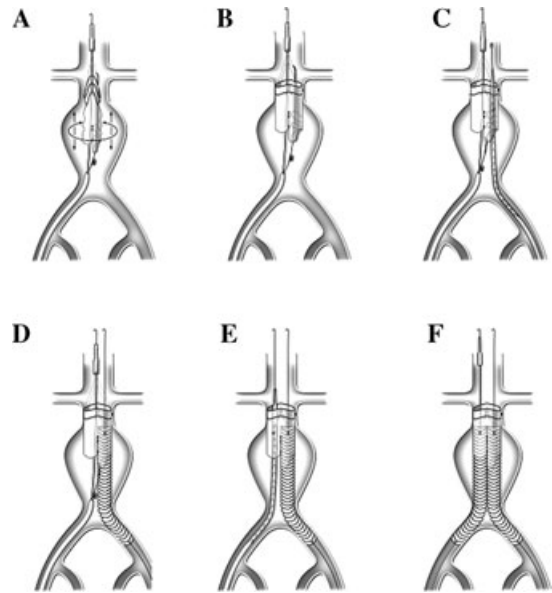
These devices guarantee the blood flow recanalization through an aneurysm by excluding the aneurysmal sac and thus preventing the rupture of the aneurysm. A stent-graft and endovascular stent and a fabric or PTFE arterial covering or lining. The stent permits to secure the proximal and distal fixation of the graft in order to anchor it to the docking area.

The first experiments with abdominal aortic stent-grafts were performed in the early 1970s by Kononov in Ukraine. Balloon-expandable stent-grafts were deployed in dogs. Volodos successfully performed the first human implantation in 1985.<sup>8</sup> However, Parodi is acknowledged as the pioneer of aortic stent-graft implantation after his first series of human deployment was published in the early 1990. It was a balloon expandable device manufactured by Barone in Argentina: Palmaz type stents are sutured to a weft-knitted polyester graft.<sup>37</sup> Since the publication of Parodi and colleagues in 1991, aortic stent-grafts have gained widespread acceptance in the treatment of both abdominal and thoracic aneurysms.<sup>9</sup> The Argentinean concept was rapidly challenged by self-expanding devices whose metallic skeleton was made of Nitinol stents or wires. The thin woven polyester weave was preferred to the knitted fabric as it can be made thinner and less porous. Expanded PTFE and polyurethane were

used as alternative to polyester. Polyurethane was rapidly abandoned because of its degradability. The risk of migration was addressed with the addition of hooks on the proximal stent. Proximal stents were left bare to permit transrenal deployment of the stent-graft. With improving advances in stent-graft technology, vascular surgeons are becoming more comfortable and more aggressive in attempting to treat the entire whole arterial tree, thanks to EVAR rapidly maturing technology.<sup>38</sup> Deployment of branched and fenestrated devices is allowing greater treatment option not only in the abdominal aorta, but in the thoracic aorta as well.<sup>39</sup>

Aneurysm of the abdominal aorta (AAA) is considered as a silent killer because it is most commonly asymptomatic. When symptoms are present, they may include: abdominal pain, pain in the lower back that may radiate, feeling of heartbeat or pulse in the abdomen. The symptoms of a ruptured aneurysm include: severe back or abdominal pain that begin suddenly and paleness, nausea, and vomiting. AAA affects as many as 8% of people over the age of 65 and 10% over 70. One in every 250 people over the age of 50 will die of a ruptured AAA. Males are four times more likely to have AAA than females. AAA is the 15th leading cause of death in USA, accounting for more than 15,000 deaths per year and the 10th leading cause of death in men over 55. Those with a family history of AAA are at a higher risk, particularly if the relative with an AAA was female.

Endovascular stent-grafting is a surgical procedure to repair the AAA of an enlarged and weakened section of an artery (Fig. 3). By using an intra-arterial sheath to place the stent-graft inside the artery, the need for open surgery is eliminated in many patients. Endovascular stent-grafting typically produces minimal discomfort and allows the patient to recover in a few days. This procedure only requires a small incision or puncture in the artery or vein. The results of this procedure lead to a shorter hospital stay, faster recovery, and less risk for the elderly patients. The patient is usually given regional anesthesia. Fluoroscopy is used to visualize the artery and guide the stent-graft placement. The physician inserts a sheath containing the pleated device over a guidewire. At the aneurysm site, the sheath containing the graft is retracted and the stent released. The stent-graft achieves its final shape through shape thermal memory or ballooning. Appropriate dock-



**Figure 3.** Different steps of deployment of the Vascutek-Terumo Anaconda stent-graft. (Courtesy of Vascutek-Terumo.)

ing of the stent-graft against the arterial wall allows blood recanalization.<sup>40</sup>

The first generation of devices was hastily conceptualized by imaginative surgeons and innovative start-ups. These developments did not necessarily incorporate the state of the art material or engineering. The metallic frames made with Nitinol were particularly ill-fated. This was primarily due to poor resistance to corrosion and inappropriate selection of sutures for their assemblage. The selection of the polymer of fabric sleeves was also less than optimal. Despite the weaknesses of the first generation of devices, endovascular aortic surgery became widely accepted at the turn of the century.<sup>41</sup> The major manufacturers recognized the potential of this technology and became involved in the development of new types of stent-grafts which resulted in a drastic increase in the quality of these devices. The new generations of Nitinol are much more corrosion resistant and the fabric and polymer selection is appropriate to the physiologic demands of such devices.<sup>42</sup> The ancillary equipment has also become much more user friendly. Today the commercially available devices offer more enhanced bi durability and biofunctionality as the direct result of the cooperation which has been forged between surgeons

and industry under the critical watch of the FDA.<sup>43</sup> In addition, to broaden the scope of the number of patients which may be considered for endovascular repair, manufacturers now propose customized devices fitted with branches or fenestrations. Thanks to the algorithm proposed by Nutley<sup>44</sup> an optimal endograft can now be selected to offer greater treatment options, treatment to a wider range of patients and ideally optimal short and long-term outcomes. Regrettably, the biocompatibility is left behind. The healing of the stent-grafts must be optimized. The interaction of the docking segment with the host artery is still poorly understood.<sup>45</sup> As endovascular surgery is here to stay, the additional contribution of engineers and basic scientists will further enhance the next generations of devices. The next challenge facing us on the horizon will be the successful recanalization of the aorta by way of a well encapsulated scaffold with a fully endothelialized flow surface.<sup>46</sup>

### Percutaneous valves

Surgical valve replacement or repair is the gold standard treatment of severe valvular heart disease. In recent years, percutaneous interventions have emerged as an alternative to surgical treatment of various valvular diseases:<sup>47</sup>

- Percutaneous pulmonary valve implantation is targeted to children, teenagers, or young adults suffering a severe pulmonary outflow tract obstruction or valvular regurgitation.
- In patients with organic mitral regurgitation (MR) due to mitral valve prolapse, direct surgical leaflet-repair techniques are typically employed in combination with implantation of an annuloplasty ring to correct the size and shape of the mitral annulus. In functional MR due to LV dilatation, mitral annulus dilation, and tethering of mitral valve leaflets, restrictive annuloplasty is employed to restore leaflet coaptation. This procedure can be achieved percutaneously by implanting a device within the coronary sinus, which is in close vicinity of the mitral annulus. The options to perform percutaneous repair of mitral leaflets are much more limited. Some devices allow edge-to-edge suture of the two leaflets in their mid-portion with the use of one or two clips delivered through a catheter. This is in fact, a percutaneous adaptation of

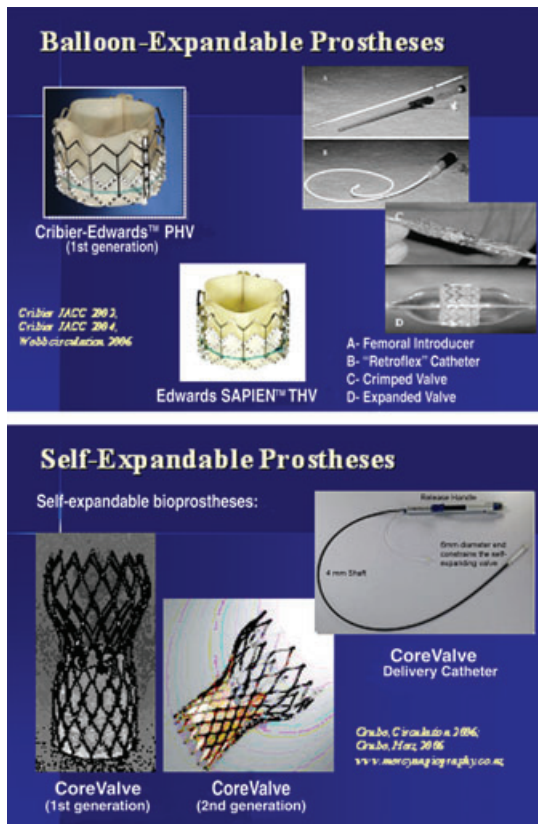
the surgical procedure proposed by Alfieri.<sup>48</sup> Because of the natural history of mitral valve diseases, these percutaneous mitral valve procedures predominantly are performed on patients aged 45–60 years old.

- Percutaneous aortic valve implantation provides an attractive alternative to standard open heart surgery in elderly patients considered to be of high or prohibitive surgical risk, in large part, due to their advanced age.

Surgical valve replacement is the gold standard treatment of severe symptomatic valve stenosis. The first human percutaneous valve replacement became a reality in 2002 by Cribier from France 10 years after<sup>11</sup> after the animal studies performed by Andersen who delivered a porcine bioprosthesis attached to a wire-based stent at various aortic sites with satisfactory hemodynamic results.<sup>49</sup> In the western countries, aortic stenosis (AS) is the most frequent cardiovascular disease after arterial hypertension and coronary artery disease. The prevalence of AS increases dramatically with age. This disease afflicts 5–7% people older than 65 years. Aortic valve replacement is the only effective treatment to reduce symptoms and extend life in patients with symptomatic severe AS. However, Decoutures and colleagues showed that 59% of patients with severe symptomatic AS older than 70 were considered at high-risk or inoperable.<sup>50</sup> For those patients, transcatheter aortic valve implantation (TAVI) may provide a promising alternative to surgical aortic valve replacement for the treatment of severe AS. The number of valve replacement surgery is expected to increase markedly in the next decade due to population aging.

There are two concepts of percutaneous valves currently available (Fig. 4). The Edwards-Sapien valve is a balloon expandable valve; it consists of three leaflets made of bovine pericardium mounted within a tubular slotted stainless-steel balloon expandable stent, 14 or 16 mm long and 23 to 26 mm diameter. Current devices require either 22 F or 24 F (transfemoral) or 26 F (transapical) sheaths for delivery. The self-expandable valve CoreValve (Medtronic, Minneapolis, MN, USA) consists of three pericardial tissues leaflets, initially bovine and currently porcine, mounted and sutured in a self-expandable nitinol stent. The available valve diameters are 22 and 26 mm. The stent frame is 50 mm





**Figure 4.** Balloon-expandable prostheses: Cribier–Edwards (first generation) and Edwards–Sapien (second generation). Depending upon the patient’s annulus diameter, that is, 18–21 mm versus 22–25 mm, a 23 mm valve via 26 mm valve is implanted. Self-expandable prostheses. Medtronic CoreValve devices: first generation and second generation. Depending upon the patient’s annulus diameter, that is, 20–23 mm versus 23–27 mm, a 20 mm valve versus 29 mm diameter valve is implanted.

long with the lower part (inflow) portion having a high radial force to expand and exclude the calcified aortic leaflets. The middle portion carries the valve and is constrained to avoid the obstruction of the coronary arteries. The outflow segment is flared to orient the stent in the ascending aorta. Early devices required a substantial 25 F delivery system. Currently available devices incorporating porcine pericardium allow a decrease in profile to 21 F. The perspective of wide use of the PHV has motivated physicians, scientists, and industry to make innovative ideas a reality. Many ingenious technologies are

at different stages of investigation and development as identified by Chiam and Ruiz.<sup>51</sup> The problem of repositioning the device is being currently addressed. Attention is focused on at the leaflets tissue engineering offers the potential for a more physiologic heart valve.

The implantations are performed with either a transfemoral or a transapical approach. The first one is performed in a catheterization laboratory by a team of interventional cardiologists and cardiac surgeons. The procedure is performed under general anesthesia or under mild sedation and local anesthesia, with transoesophageal echocardiography, and without cardiopulmonary bypass (except for rare cases). Balloon aortic valvuloplasty is performed before valve implantation. The mounted valve is positioned using fluoroscopic, aortographic, and echocardiographic guidance. It is expanded under rapid pacing (180–200 beats/min) to minimize transvalvular flow and the risk for valve embolization.<sup>52,53</sup> The transapical approach is performed in the surgical operating room or hybrid room, under transoesophageal echocardiographic and fluoroscopy guidance, without cardiopulmonary bypass. Balloon valvuloplasty is performed under rapid pacing in all patients before valve implantation. Postballoon dilation with a larger balloon is performed in case of a moderate to severe paravalvular leak.<sup>6</sup>

At the present time, only patients considered at high or prohibitive risk for open surgical aortic valve replacement are eligible for transcatheter procedures. Approximately 30% of patients who have a class I indication for surgical aortic valve replacement are not referred to surgery. The main reasons for this phenomenon are the advanced age of the patients and the presence of multiple comorbidities. The vast majority of these patients are eligible for transcatheter valve implantation. The first step is to determine if the patient is eligible for transcatheter implantation based upon an algorithm. The next step is the selection of the bioprosthesis diameter based on the size of the aortic annulus root diameter measured by transoesophageal echocardiography:

- Sapien valve: The 23-mm valve is selected if the aortic annulus diameter is between 16 and 21 mm, and the 26-mm valve is selected if the aortic annulus diameter is between 22 and 25 mm.



**Table 1.** Clinical results published in the literature for the Sapien–Edwards and the CoreValve

Reference	Number of patients	Age (years)	NYHA		Device/ approach	Procedural success (%)	30-Day mortality (%)
			functional class	Logistic Euroscore			
Cribier <i>et al.</i> 2006	35	80 ± 7	100	12 ± 2	Edwards TF*	75	23
Webb <i>et al.</i> 2007	50	82 ± 7	90	28	Edwards TF	86	12
Lichtenstein <i>et al.</i> 2006	7	77 ± 9	85	35 ± 26	Edwards TA	100	14
Walther <i>et al.</i> 2008	50	82 ± 5	100	28 ± 12	Edwards TA	94	8
Grube <i>et al.</i> 2006	25	80 ± 5	96	11 ± 3	CoreValve TF	88	20
Marcheix <i>et al.</i> 2007	10	81	100	32 ± 15	CoreValve TF	100	20

NYHA, New-York Heart Association; EuroSCORE, European System for Cardiac Operative Risk Evaluation; TF, transfemoral; TA, transapical; \*Delivery of the valve was performed by an antegrade trans-septal (26 patients) or retrograde approach (7 patients).

- CoreValve: The 26 mm valve is selected if the aortic annulus diameter is between 20 and 23 mm and the aortic root diameter  $\geq 27$  mm and the 29 mm and the aortic root diameter  $\geq 28$  mm.

The third and final step is to select the implantation approach. This applies only to the Sapien–Edwards valve. The transfemoral approach is selected unless one of the following criteria is present:

- Femoral or iliac arteries diameter are too small for sheath introduction (<7 mm: 23 mm Sapien valve, <8 mm: 26 mm Sapien valve).
- Femoral or iliac tortuosity and calcification too significant for catheter transit.
- Horizontal or heavy calcification of ascending aorta which may lead to an increased risk of embolization.

More than 6000 patients have received a percutaneous valve worldwide. The longest follow-up is currently 4 years without bioprosthesis or stent failure (Table 1). Because of the advanced age of this population, only a few patients have completed follow-up during that time interval. There is an important learning curve and several studies have reported that the results of the procedure improve significantly with the number of cases performed. Successful implantations are >85% for both available models of percutaneous valves. Thirty-day mortality varies between 6% and 20% depending on the series and the implantation approach.<sup>54–57</sup> Table 1 shows the clinical results published in the literature for the Sapien–Edwards implanted by the transfemoral approach.

The Sapien–Edwards is performed by the transapical approach, and the CoreValve by the transfemoral approach respectively. This new technology is predominantly used in the elderly population; the average age of the different studies was between 77 and 82 years. On average, transfemoral approach was associated with lower 30-day mortality and better late survival. This difference may be related to selection biases (*i.e.*, patients with transapical approach generally have a worse risk profile) and/or to the relatively more invasive nature of the transapical procedure. Hemodynamic performance of percutaneous bioprostheses is excellent with a mean transvalvular gradient <10 mmHg and an aortic valve area >1.5 cm<sup>2</sup> in most cases. When compared to standard bioprostheses implanted by surgical aortic valve replacement, percutaneous valves had better performance in terms of gradients and aortic valve areas.<sup>9</sup> On the other hand, they were associated with a higher incidence of perivalvular aortic regurgitation. One of the important questions that remained unanswered until recently is what will be the durability of percutaneous bioprostheses and how will this compare to that of surgical bioprostheses.

It is expected that this new technology will rapidly develop especially in the elderly population, which generally has a higher operative risk with the use of standard aortic valve replacement. On the other hand, the widespread use of transcatheter valve implantation may be more limited in the younger population due to the relatively high incidence of perivalvular regurgitation and the lack of data with respect to its long-term durability.

## Conclusion

Implantable cardiovascular devices, that is, signal prostheses and conduction prostheses that can be deployed percutaneously, represent a most extraordinary revolution in the treatment of cardiovascular illnesses.<sup>58,59</sup> According to Dhruva, in 2008 at least 350,000 pacemakers, 140,000 cardioverter—defibrillators, and 1,230,000 stents were implanted in the United States.<sup>60</sup>

Half a century has elapsed since the first pacemaker implantation, paving the way for sophisticated devices which can provide electrical pulse transmission that support the mechanical function of the heart. The technology has matured progressively, and a variety of devices now provide treatment options for multiple forms of arrhythmias. Pacemaker implantations are now well accepted for the treatment of elderly patients;<sup>61</sup> the same is now also true for defibrillators.<sup>62,63</sup>

Arterial reconstruction or optimization of blood flow by percutaneous renewal of the arterial tree of the heart valves represents the most remarkable achievement of the last 30 years. Innovations were mostly physician-driven and based on a willingness to treat frail elderly patients. Thanks in part to massive investments from industry, together with greater imaging capacities, deployment of percutaneous devices to treat these complicated pathologies have matured rapidly (stents) or are still maturing (stent-graft).<sup>64</sup> We can anticipate further outstanding developments of percutaneous devices to treat valvular pathologies as well.<sup>65</sup>

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## Conflicts of interest

The authors declare no conflicts of interest.

## References

- Schneider, P. 2009. Innovations in surgical practice: where do they come from and what do they mean? In *Proceedings of the 31st Annual Meeting of the Canadian Society for Vascular Surgery*. Ottawa, Canada. September 25–26.
- Senning, A. 1964. On the use of electric pacemakers in the treatment of Adams–Stokes syndrome. *Langenbecks Arch. Klin Chin Ver Dtsch Z. Chir.* **308**: 265–273.
- Panotopolos, P.T. *et al.* 1997. Efficiency of the implantable cardioverter-defibrillator in the elderly. *J. Am. Coll. Cardiol.* **29**: 556–560.
- Dotter, C.T., M.P. Judkins & J. Rösch. 1969. Transluminal angioplasty in arteriosclerotic obstruction of the lower extremities. *Med. Times* **97**: 95–108.
- Grüntzig, A. 1978. Transluminal dilatation of coronary-artery stenosis. *Lancet* **1**: 263.
- Palmaz, J.C. 1988. Balloon-expandable intravascular stent. *Am. J. Roentgenol.* **150**: 1263–1269.
- Carrié, D. *et al.* 2000. Ten-year clinical and angiographic follow-up of coronary wallstent. *Am. J. Cardiol.* **85**: 95–98.
- Vossoughi, J. 2000. Historical development of stent-graft. Pp. 15–21 in J. Vossoughi, N. Kipshidze & J. W. Karanian (eds.), *Stent-Graft Update*. Washington, DC: Medical and Engineering Publishers Inc.
- Parodi, J.C., J.C. Palmaz & H.D. Barone. 1991. Transfemoral intraluminal graft implantation for abdominal aortic aneurysm. *Ann. Vasc. Surg.* **5**: 491–499.
- Blum, U. *et al.* 1996. Abdominal aortic aneurysms: preliminary technical and clinical results with transfemoral placement of endovascular self-expanding stent-grafts. *Radiology* **198**: 25–31.
- Cribier, A. *et al.* 2002. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case human description. *Circulation* **106**: 3006–3008.
- Jahangir, A., W.K. Shen. 2003. Pacing in elderly patients. *Am. Heart J.* **146**: 750–753.
- Abrahams, J. *et al.* 2002. ACC/AHA/NASPE Guideline update for implantation of cardiac pacemakers and antiarrhythmia devices. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/NASPE Committee on Pacemaker Implantation). ACC: [www.acc.org](http://www.acc.org); AHA: [www.americanheart.org](http://www.americanheart.org); NASPE: [www.naspe.org](http://www.naspe.org)
- Gregoratos, G. 1999. Permanent pacemakers in older persons. *J. Am. Geriatr. Soc.* **47**: 1125–1135.
- Payne, G.E. & J.D. Skehan. 1994. Issues in cardiac pacing: can ageism be justified? *Br. Heart J.* **72**: 102–103.
- Schmidt, B. *et al.* 2004. Pacemaker therapy in very elderly patients: long-term survival and prognostic parameters. *Am. Heart J.* **146**: 908–913.

17. Shen, W-K. *et al.* 1996. Survival and functional independence after implantations of a permanent pacemaker in octogenarians and nonagenarians: a population bases study. *Ann. Int. Med.* **125**: 476–480.
18. McComb, J.M. & R.S. Bexton. 1995. Permanent pacemakers in the elderly: concerns, costs and benefits. *Br. Heart. J.* **74**: 9–10.
19. Mirowski, M. *et al.* 1982. Implantable automatic defibrillators: their potential in prevention of sudden coronary death. *Ann. N.Y. Acad. Sci.* **382**: 371–380.
20. Zipes, D. *et al.* 2006. European Heart Rhythm Association. Heart Rhythm Society, American College of Cardiology, American Heart Association Task Force, European Society of Cardiology Committee for Practice Guideline. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). *Circulation* **114**: e385–e484.
21. Healey, J.S. *et al.* 2007. Role of the implantable defibrillator among elderly patients with a history of life-threatening ventricular arrhythmias. *Eur. Heart J.* **28**: 1746–1749.
22. The Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. 1997. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. *N. Engl. J. Med.* **337**: 1576–1583.
23. Buxton, M. *et al.* 2006. A review of the evidence on the effects and costs of implantable cardioverter defibrillator therapy in different patient groups and modeling of cost-effectiveness and cost-utility for these groups in a UK context. *Health Technol. Assessment* **10**: 1–184.
24. Bardy, G.H. *et al.* 2005. Sudden Cardiac Death in Heart Failure trial (SCD-Het) investigators. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N. Engl. J. Med.* **352**: 225–237.
25. Goldenberg, Z. & R. Lampert. 2006. Implantable cardioverter-defibrillators. *Expanding indications and technologies. JAMA* **295**: 809–818.
26. Epstein, A.E. *et al.* 2009. Implantable cardioverter-defibrillator prescription in the elderly. *Heath Rhythm* **6**: 1136–1143.
27. Wan, S. & M.J. Underwood. 2007. *Cardiovascular surgery in the aging world 2007 Year Book of the Intensive Care and Emerging Medicine*. Pp. 447–430 in Intensive Care, Berlin, Heidelberg: Springer.
28. Grüntzig, A.R., A. Senning & W.E. Siegenthaler. 1979. Non-operative dilatation of coronary artery stenosis: percutaneous transluminal coronary angioplasty. *N. Engl. J. Med.* **301**: 61–68.
29. Dorros, G. *et al.* 1983. Percutaneous transluminal angioplasty: report of complications from the National Heart Lung and Blood Institute. PTCA registry. *Circulation* **67**: 723–730.
30. Palmaz, J.C. 2004. Intravascular stents in the last and next 10 years. *J. Endovasc. Ther.* **11**(Suppl 2): II-200–II-206.
31. Mani, G. *et al.* 2007. Coronary stents: a materials perspective. *Biomaterials* **28**: 1689–1710.
32. Grüntzig, A. 1981. Percutaneous transluminal angioplasty. *Ann. Roentgenol.* **136**: 216–217.
33. Haery, C, R.S. Sachar & S.G. Ellis. 2004. Drug-eluting stents: the beginning of the end of restenosis? *Clev. Clin. J. Med.* **71**: 815–824.
34. Berger, P.B. *et al.* 1999. Clopidogrel versus Ticlopidine after intracoronary stent placement. *J. Am. Coll. Cardiol.* **34**: 1891–1894.
35. Colombo, A. & E. Karvouni. 2000. Biodegradable stents—“Fulfilling the mission and stepping away”. *Circulation* **102**: 371–373.
36. Walksman, R. 2007. Promise and challenges of bioresorbable stents. *Catheter Cardiovasc. Interv.* **70**: 407–414.
37. Parodi, J.C. 2002. Eleven years of endografts: what have we learned? *Acta Chir. Belg.* **102**: 289–291.
38. Marin, M.L. *et al.* 2003. Endovascular stent-graft repair of abdominal and thoracic aortic aneurysms: a ten-year experience with 817 patients. *Ann. Surg.* **238**: 586–595.
39. Greenhalgh, R.M. & J.T. Powell. 2008. Endovascular repair of abdominal aortic aneurysm. *N. Engl. J. Med.* **358**: 494–501.
40. Guidoin, R. *et al.* 2008. Transrenal deployment of a modular stent-graft to repair AAAs with short neck: experiments in dogs. *Artif. Cells Blood Substit. Immobil. Biotechnol.* **36**: 310–339.
41. Vallabhanessi, S.R. & P.L. Harris. 2001. Lessons learn from the Eurostar registry on endovascular repair of abdominal aortic aneurysm repair. *Eur. J. Radiol.* **39**: 34–41.
42. Guidoin, R. *et al.* 2004. Biocompatibility studies of the Anaconda stent-graft and observations of nitinol corrosion resistance. *J. Endovasc. Ther.* **11**: 385–403.
43. Chaikof, E.L. *et al.* 2009. Society for Vascular Surgery. The care of patients with an abdominal aortic aneurysm:

- the Society for Vascular Surgery practice guidelines. *J. Vasc. Surg.* **50**: S2–S49.
44. Nutley, M. *et al.* 2009. Anatomic approach to endograft selection for the treatment of AAA. In *Proceedings of the 31st Annual Meeting of the Canadian Society for Vascular Surgery*. Ottawa, Canada. September 25–26.
  45. Noishiki, Y. *et al.* 2001. Introduction of tissue engineering concepts into the field of endovascular grafts: an attempt to solve endoleakage problems of endovascular grafts implanted in aortic aneurysms. *Art. Organs.* **25**: 228–235.
  46. Guidoin, R. *et al.* 2009. Analysis of explanted Late-cba modular stent-grafts deployed transrenally to repair AAAs with short necks in 29 dogs. *Artif. Cells Blood Substit. Immobil. Biotechnol.* **37**: 23–31.
  47. Bonow, R.O. *et al.* 2006. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing Committee to Revise the 1998 Guidelines for the management of patients with valvular heart disease) developed in collaboration with the Society of Cardiovascular Anesthesiologists endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. *J. Am. Coll. Cardiol.* **48**: e1–e148.
  48. Alferi, O. *et al.* 2007. Future directions in degenerative mitral valve repair. *Semin. Thorac. Cardiovasc. Surg.* **19**: 127–132.
  49. Andersen, H.R., L.L. Knudsen, J.M. Hasenkam. 1992. Transluminal implantation of artificial heart valves. Description of new expandable aortic valve and initial results with implantation by catheter technique in close chest pigs. *Eur. Heart J.* **13**: 704–708.
  50. Descoutures, F. *et al.* 2008. Contemporary surgical of percutaneous management of severe aortic stenosis in the elderly. *Eur. Heart J.* **29**: 1410–1417.
  51. Chiam, P.T., C.E. Ruiz. 2009. Percutaneous transcatheter aortic valve implantation: Evolution of the technology. *Am. Heart J.* **157**: 229–242.
  52. Webb, J.G. *et al.* 2006. Percutaneous aortic valve implantation retrograde from the femoral artery. *Circulation* **113**: 842–850.
  53. Grube, E. *et al.* 2006. Percutaneous implantation of the Core Valve self-expanding valve prosthesis in high-risk patients with aortic valve disease: the Siegburg first-in-man study. *Circulation* **114**: 1616–1624.
  54. Lichtenstein, S.V. *et al.* 2006. Transapical transcatheter aortic valve implantation in humans: initial clinical experience. *Circulation* **114**: 591–596.
  55. Rodés-Cabau, J. *et al.* 2008. Feasibility and initial results of percutaneous aortic valve implantation including selection of the transfemoral or transapical approach in patients with severe aortic stenosis. *Am. J. Cardiol.* **19**: 304–310.
  56. Webb, J.G., S. Lichtenstein. 2007. Transcatheter percutaneous and transapical aortic valve replacement. *Semin. Thorac. Cardiovasc. Surg.* **19**: 304–310.
  57. Clavel, M.A. *et al.* 2009. Comparison of the hemodynamic performance of percutaneous and surgical bioprostheses for the treatment of severe aortic stenosis. *J. Am. Coll. Cardiol.* **53**: 1883–1891.
  58. Kirsch, M. *et al.* 1998. Cardiac operations in octogenarian: perioperative risk factors for death and impaired autonomy. *Ann. Thorac. Surg.* **66**: 60–67.
  59. Gatti, G. *et al.* 2002. Predictors of postoperative complications in high-risk octogenarians undergoing cardiac operations. *Ann. Thorac. Surg.* **74**: 671–677.
  60. Dhruva, S.S., L.A. Bero, R.F. Redberg. 2009. Strength of study evidence examined by the FDA in premarket approval of cardiovascular devices. *JAMA* **302**: 2679–85.
  61. Gregoratos, G. 2005. Indications and recommendations for pacemaker therapy. *Am. Fam. Physicians* **71**: 1563–1570.
  62. Huang, D.T. 2007. For the MADIT-II research Group. Improved survival associated with prophylactic implantable defibrillators in elderly patients with prior myocardial infarction and depressed ventricular function: a MADIT-II substudy. *J. Cardiovasc. Electrophysiol.* **18**: 833–838.
  63. Pellegrini, C.N. *et al.* 2008. Impact of advanced age of survival in patients with implantable cardioverter defibrillators. *Europace* **10**: 1296–1301.
  64. Torella, F. 2004. On behalf of the Eurostar collaborators. Effect of improved endograft design on outcome of endovascular aneurysm repair. *J. Vasc. Surg.* **40**: 216–221.
  65. Block, P.C. 2009. Transcatheter aortic valve replacement: here and now, but lots to learn. *J. Invasive Cardiol.* **21**: 99–100.