

# Reducing fear and the risk of death in Marfan syndrome: a Chaucerian pilgrimage

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## Prologue

**C**haucer's characters in *The Canterbury Tales* meet on their journey to the shrine of Thomas à Becket. They are on a pilgrimage, a special kind of journey that brings a diverse group of people together in a common purpose. As they converge on the place of pilgrimage, the tales they tell are informed by the varied experiences of their lives. The stories we tell here are of individuals brought together by a single objective: to find a solution better than total root replacement for people whose lives are threatened by aortic dilatation due to Marfan syndrome. Chaucer's pilgrims meet in the Tabard Inn in Southwark, where their journey to Canterbury is to begin. This modern journey began in St George's Hospital at the 2000 meeting of the Marfan Association, when the surgeon [TT] told his tale, an account of best current practice and its attendant risks.

**Key words:** Marfan syndrome, aortic root replacement, valve sparing.

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## The surgeon's tale

*A surgeon came, and with him, for the aid  
Of sufferers, brought the tackle of his trade,  
His forceps, knife and lancet, and a saw.  
For opening the chest. His smock he wore,  
For he that morning from the brink of death  
Had pulled one such, and since had scarce drawn breath...*

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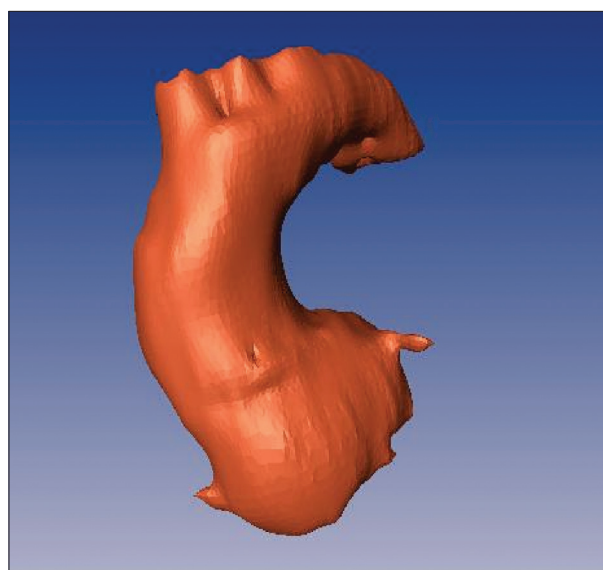
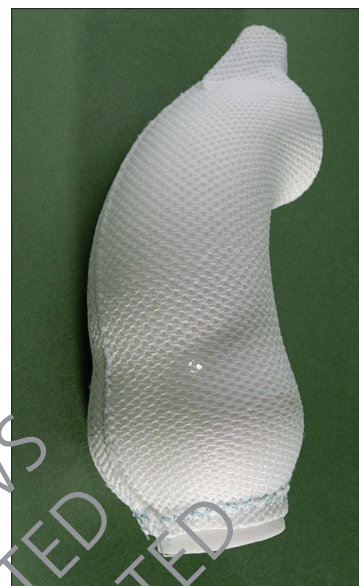
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The single most threatening manifestation of Marfan syndrome is aortic root dilatation, dissection and rupture. If left to nature, this is the most common cause of death in Marfan patients, killing two thirds of them, often in their twenties or thirties. Bentall proposed the first effective solution and his name is given to the operation of replacement of the aortic root and the ascending aorta with a durable prosthetic tube graft and a mechanical valve. This is the present standard of care; it can be performed with low risk and offers prolongation of life to many patients with Marfan syndrome.<sup>1</sup> As aortic root surgery has been made safer, surgeons have felt entitled to offer replacement earlier in the progression but there is no escaping the fact that this is major surgery.

Root replacement carries with it the risks inherent in the use of cardiopulmonary bypass. In order to remove the entire ascending aorta, the surgeon often uses profound hypothermia (as cold as 18°C) and a period of total circulatory arrest. With the heart and aorta widely opened up to the arch, there is a risk of cerebral air embolism. The coronary arteries have to be re-implanted and any accident or technical error may result in myocardial infarction. All the arterial tissues are fragile and post-operative bleeding is a major anxiety. The risks do not stop with recovery from surgery. If a mechanical valve has been implanted (which provides the most durable solution), life-time anticoagulation is mandatory so the patient's life is bounded on one side by risk of embolism and on the other by fear of bleeding.

Conserving the valve during total replacement of the ascending aorta is possible but is achieved by only a minority of surgeons. Without doubt, this adds greatly to the difficulty of the operation. The factory-made valved conduit is at least a reproducible and reliable product, whereas re-supporting the three cusps of the native valve within a prosthetic tube graft requires a high level of craftsmanship, in surgery performed against the clock, on an ischaemic heart. Time on bypass adds incrementally to damage to the brain, the blood, the heart and other sensitive organs. To try and then to fail adds time to no advantage. Having conserved the valve, the surgeon still fears failure with the need for future surgery.

An attractively conservative alternative that was suggested many years ago is to wrap the aorta with graft material cut and sewn intra-operatively and fashioned externally to prevent expansion. Photographs of the operation show it to be disappointingly crude, however, and the medium-term results have been poor. Taking everything into account, the best that could be offered in 2000 was regular echocardiographic monitoring of the aortic root with a view to elective surgical replacement of the

**Figure 1.** Computer-aided design model of Marfanoid ascending aorta**Figure 2.** The porous mesh exostent (on its manufacturing former)

root (with or without the aortic valve) according to criteria based on absolute size, rate of change and family history.<sup>2,3</sup> The surgeon's tale included his own work in devising patient-specific nomograms against which to monitor an individual's aortic dimensions over time.<sup>4,5</sup> This adds some sophistication but it is still an exercise in brinkmanship.

Nevertheless, many patients are grateful for the chance to survive and at the Marfan Association meeting there were mothers who had brought their darling sons to him to have the operation in their gap year. Demonstrating enormous trust, they asked for their children to have this life-prolonging operation behind them as they embarked on their adult lives away from home.

### The engineer's tale

*An engineer, whose working days were spent  
On figuring and hairsbreadth measurement  
And instruments of intricate design,  
Having a notion that one might confine  
The swelling artery with an armlet strong  
But pliant, with the surgeon rode along...*

The engineer (TG) heard the surgeon's tale. It was clear that some of the measurements that an engineer might like to make, such as the tensile strength of aortic tissues, were close to impossible, so experience and pragmatism had to be relied upon. Somewhat surprisingly to the engineer, who knew of the elegance of Leonardo da Vinci's theories and drawings, present-day surgical solutions were crude. An off-the-shelf tube graft (whether or not the surgeon was attempting to conserve the valve cusps) was the best that could be provided. Performance of conventional composite aortic root grafts indicated that the body

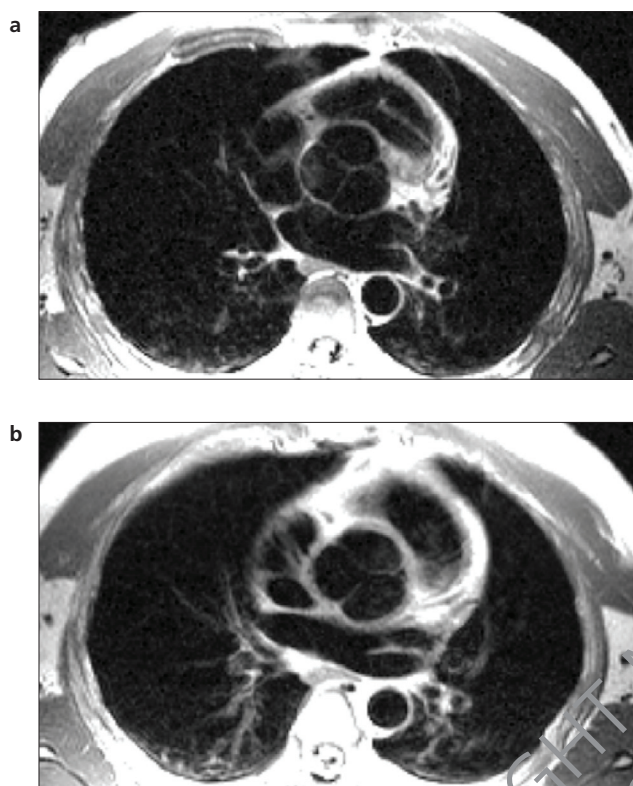
could accept what, in hydraulic terms, is a substantially rigid replacement of the compliant, pressure-accumulating natural aorta. The body was clearly more tolerant than he might have imagined. There was room for manoeuvre for the engineer, and plenty of scope for improvement on the surgeon's best offer to date.

The engineer's vision was that he could support but not excise the aorta. If this were done much earlier, at a size where the valve functioned and the aorta had not yet thinned and dilated, he saw a way to conserve all the natural tissues. He knew how to make a replica of the aorta by sculpting a model from the digital information obtained from non-invasive imaging.

Given the problems with X-rays and the limitations of images from echocardiography, magnetic resonance imaging (MRI) was chosen. Taking MRI data of the ascending aorta is complicated by the motion of the heart and associated structures but it was achieved. It takes time, patience and expertise but it is entirely safe – unlike having to employ all your resources of craftsmanship on the operating table in a race against a time-related loss of irreplaceable neurons and myocytes. Once acquired, MRI digital information was used in a computer-aided design (CAD) process. Iteration around the imaging-CAD modelling loop finally resulted in a scanning protocol that did not over-stress the patient but did provide sufficient dimensional/morphological data from the ascending aorta to allow a suitably accurate CAD model to be produced (figure 1).

With the imaging and CAD modelling validated, there was an appropriate model of the patient's aorta. Converting the CAD model into a life-size replica of the aorta was achieved using a modern rapid prototyping (RP) technique that allows one-off physical models to be produced at low cost.

**Figure 3.** **a:** Pre- and post-operative **b:** transverse MRI images of the aortic valve



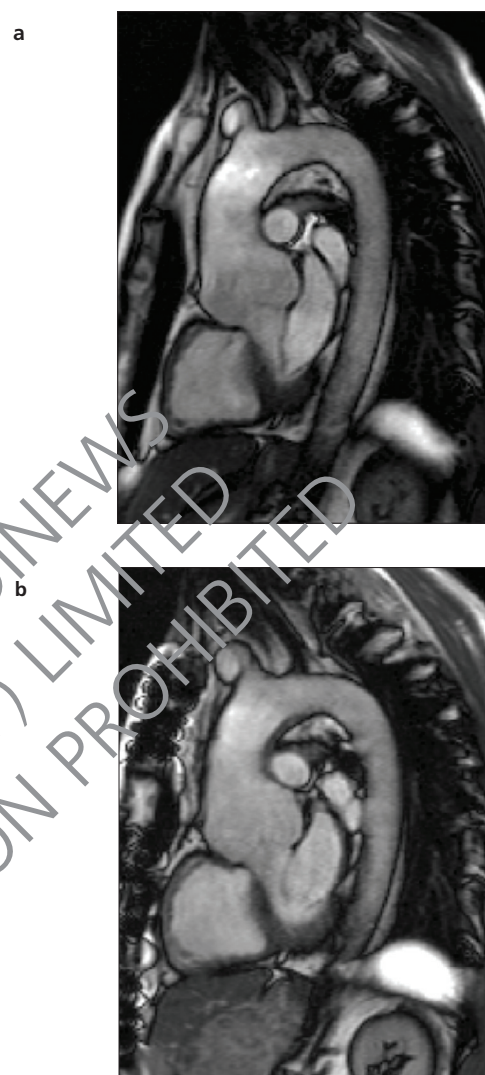
**Key:** MRI = magnetic resonance imaging

Polyester (as used in dacron grafts), tried and tested over many years of clinical experience, was an obvious choice of material, which required no further experimentation or development. Since the aorta was to be left in place, with the critical blood-endothelium interface completely preserved, the external support (or exostent) could be porous. In fact, this probably made it better, since it could be incorporated and provide no obstruction to tissue fluids. With an accurate physical model of the patient's aorta, the porous mesh exostent was formed on it. Development of the stent specification resulted in a highly porous, lightweight, textile mesh in a medically approved polymer, perfectly formed to the morphology of the aortic model (figure 2). Cleaning, sterilising and packing followed prior to the surgeon implanting the device.

#### The sufferer's tale

*A sufferer, lean-faced and long of limb,  
Was in their company, with eyesight dim  
For that his eye did flicker to and fro.  
His father, a tall narrow man also,  
Too soon, in spite of his physician's art,  
Had died with this affliction of the heart...*

**Figure 4.** Pre- **a:** and post-operative **b:** MRI images of the aortic root and ascending aorta (TJG)



**Key:** MRI = magnetic resonance imaging

*Hearing the surgeon and the engineer  
Gave him new hope. He tells his own tale here...*

I became aware of Marfan syndrome as a six-year-old at the ophthalmic clinic at Cheltenham General Hospital; like my father I had very poor eyesight. When I was 35 years old (in 1992) I participated in a genetic study of Marfan syndrome with my father only to find that my aortic root diameter was already 4.4 cm ('normal' being 3.2 to 3.6 cm). The repeated stress of annual echo measurements prompted basic animal fear, which alternated with denial. By 1999 my aorta was approaching 5 cm.

My GP persuaded me to take a beta blocker (atenolol 50 mg daily) and a diuretic (bendrofluazide 5 mg daily), with the ratio-



nale that reduction in my mean blood pressure and the rate of rise of the pressure wave might slow the processes of medial destruction in my fibrillin-deficient aorta. For someone who was living a very active life, accepting a drug-supported existence was very difficult, notwithstanding the relatively benign drugs involved.

I heard the surgeon's tale. After considering the composite aortic root graft and the less reliable valve preservation procedures, I was unenthusiastic about the degree of physical intrusion they both represented. I was highly averse to permanent anticoagulation therapy. I was struck by how wasteful it was to discard the ascending aorta with its biological compatibility and beautiful haemodynamic internal morphology (Marfanoid dilation notwithstanding) for the sake of a little tensile strength. The engineer's tale seemed to hold a better solution to this problem. To support my own tissue was preferable.

Hearing the surgeon's tale in March 2000 provided an opportunity to quiz someone who not only understood the surgery, but was open-minded enough to consider alternative treatments. I assembled a core technical team comprising the surgeons Tom Treasure and John Pepper, and Michael Lampérth and myself as the engineers.

Writing a project proposal was no problem except that it was essentially an engineering proposal for application in the world of medicine, so cross-discipline technical jargon was something of a challenge. It did not interest the British Heart Foundation sufficiently to raise any funds so we relied on private investors. "What happens if you die?" asked one prospective investor. "Hard luck: you lose your money," was my only response.

The project started for real in September 2002. On May 24th 2004 the External Aortic Root Support project concept was, in engineering terms, proven when John Pepper installed the first bespoke exostent around my aorta.<sup>6</sup>

Post-operative echo and MRI scans (figures 3 and 4) show my aorta to be of stable diameter and still reasonably compliant, better approximating the natural aorta than the composite aortic root graft. I require no medication. Should there be any requirement for further intervention, all my original tissues are present; no bridges have been burned. All currently available procedures can still be performed and, indeed, an aorta encased in this exostent probably offers the surgeon more security than an unsupported Marfan aorta.

Mental stress is hard to quantify but relief from it has added immeasurably to my quality of life. Having conceived and been at the centre of this project from the start, my next task is to persuade the rest of the medical world of its merit.

## Epilogue

What are the means by which we make changes in surgery? How have we accommodated surgical innovation? Viewed from our present day perspective, particularly if we make the simple assumption that what we do now is right, we can trace events backwards, seeking out who did what first. This leads to a reading of history as medical triumphalism.<sup>7</sup> This Whiggish view of progress, ever onwards and upwards, often fits the facts poorly.

The truth is that the footprints we see now pointing in our direction can only be identified from a knowledge of where we now stand. In fact they are surrounded by many others. These are the footprints marking false starts, the journeys that petered out, and many pointing in other directions.

We may not be able to learn much from history but we learn nothing if we do not study it, reflect upon it and explore how history allows us to understand our own time more fully. Sometimes medical innovation is a story of perseverance and tenacity but more often it is a lucky event or a serendipitous combination of circumstances. Both open-heart surgery and antibiotics were improbable outside chances in 1940. Gibbon took 22 years (1931–1953) to make his idea of a heart-lung machine work on a patient, a story of tenacity, but it was the chance observation of a penicillin mould inhibiting bacterial growth that led Fleming to antibiotics.<sup>8</sup> (There was more hard work in it than that but the story of penicillin "still had the power to amaze."<sup>8</sup>)

In our view, the engineered solution to containing the Marfan's aorta was more than a chance meeting of minds. Apparent chance discovery may be assisted. Opportunity for improvement and progress provided by being open to ideas from other disciplines, often called cross-fertilisation, requires listening to others' tales. As we become more and more specialised we have less and less opportunity to hear work outside our own experience. Telling this story as three tales illustrates the process. But there is a more culpable obstacle to innovation than the lack of opportunities to hear alternative points of view; that is the rejection from consideration of all that is challenging or from outside our existing sphere of knowledge and our assumptions. It may be laudable (at least up to a point) to be questioning, sceptical, challenging and even overtly critical of new and alien concepts; this is the style that we teach to our medical students. Given that tradition of scepticism, we should hardly be surprised when mature colleagues rise to challenge this concept with little apparent time for thought.<sup>9</sup>

For many years the three tale tellers have individually studied and thought about the surgery of this condition. Over the five years since the surgeon's and engineer's views of the Marfan's aorta came into the same focus, we have spent many hours discussing between ourselves and with others all the imaginable implications and pitfalls. The first operations have been performed with immediate success; only with passage of time will we be able to prove conclusively that what we offer now is better than what went before.

In the case of management of the Marfan aorta it is not as if the present approach is perfect. Root replacement has immediate and long-term risks. Consider the surgeon's tale again. If we intervene too early, the immediate risk taken may not be necessary and the long-term risks have to be borne for longer. If the aorta dissects, the results are disastrous and we have missed the boat. It is an exercise in brinkmanship. We believe we have found a better way.

## Acknowledgement

Prologues to the surgeon's tale, the engineer's tale and the



### Key messages

- The single most feared manifestation of Marfan syndrome is aortic root dissection and rupture
- The present standard is total root and valve replacement as a pre-emptive operation (Bentall's operation)
- Sparing the valve is one of the goals of pioneering surgery
- Total tissue sparing can be achieved with a customised external support
- Low-risk elective surgery has the potential to greatly reduce anxiety and improve quality of life

patient's tale were provided by Joe Treasure (after Geoffrey Chaucer). © Joe Treasure 2006.

### Conflict of interest

Undeclared

### Further information

The Marfan Association UK was established in 1984 to offer sup-

port, education and research, working with patients and medical teams across the country.

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