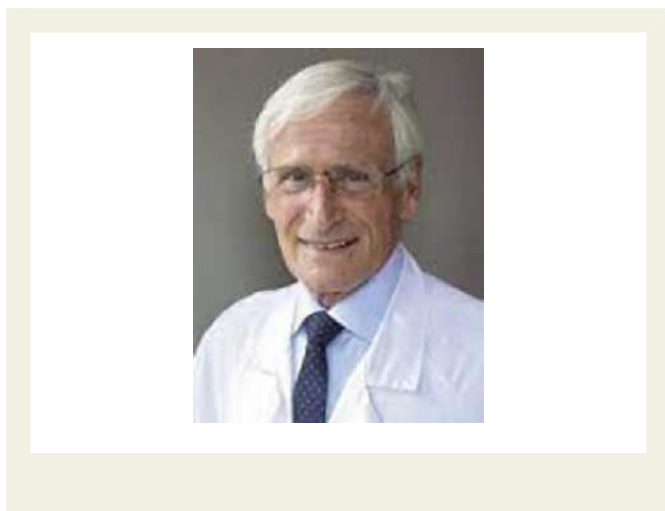


## In Memoriam

# In memoriam: Alain Cribier

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Cardiology has suffered the loss of one of its greatest physicians. In every generation, visionaries have understood the specific clinical challenges of their time and responded with solutions that have changed the paradigm for treating life-threatening diseases. Alain Cribier was one of them. Professor Alain Cribier revolutionized the treatment of heart valve disease. With the percutaneous aortic valve implantation (TAVI), he saved several thousand patients and changed the treatment of structural heart disease.

Alain Cribier was born in Paris, France, in 1945. He studied medicine at the University of Paris. He grew up with a passion of music and brilliantly mastered the piano, but he also had an early determination to pursue the medical profession—inspired, among others, by the physician–musician, philosopher, and Nobel Peace Prize laureate Albert Schweitzer, whom he met in Alsace in his early youth and by William Ganz and Jeremy Swan at Cedars-Sinai Medical Center, Los Angeles, CA, USA, during his 1-year fellowship. Afterwards, he joined Pr Brice Letac at the Rouen University Hospital in France in 1972 as an interventional cardiologist, before becoming head of the cardiology department.

Alain Cribier could no longer stand seeing patients with aortic stenosis who were contraindicated for surgical replacement die. He created

the technique of ‘balloon aortic valvuloplasty’ (BAV), which involves dilating the narrowed and calcified aortic valve by inflating a balloon using standard catheterization techniques under local anaesthesia. The application of balloon valvuloplasty to calcific aortic stenosis was, however, a major challenge due to concerns on the possibility to improve valve function in the presence of extensive calcification, which is the major determinant of the disease. Although this concept was considered unrealistic, Prof. Cribier believed in his approach and was able to successfully perform the very first case in September 1985 in Rouen on a very symptomatic 72-year-old woman. When this first BAV resulted in a spectacular clinical improvement, allowing the patient to return to a normal life, the publication of this first series of Rouen in 1986 in *The Lancet* aroused international enthusiasm within the medical community and led to a rapid worldwide spread of this technique with hundreds of patients and cardiologists from all over the world coming to Rouen to be treated or learn the technique.

Balloon aortic valvuloplasty was subsequently evaluated in major international registries in Europe and the USA and was the subject of hundreds of articles. However, after a few years, it was identified that the clinical benefits were not lasting due to early restenosis of the valve.

Professor Alain Cribier did not abandon, convinced that percutaneous treatment of calcific aortic stenosis remained possible. It was at this time that he developed the TAVI concept. He had in mind a balloon-expandable stent including the leaflets of a bioprosthesis with enough strength to push away the diseased native calcified valve and to maintain valve opening, the native valve being used as an anchor to the stent. The dimensions of the stent were chosen to avoid compromising the function of adjacent structures. This bioprosthesis had to be introduced by percutaneous approach. His concept came from his observation that, during balloon dilatation, the balloon could be fully inflated and in a circular fashion, thus pushing away the diseased calcified native valve. He began to explore this idea at the end of the 1980s, at the same time as he was confronted with early post-aortic valvuloplasty (AV) valve restenosis.

During 5 years, the search for biomedical companies interested in this concept and willing to engineer and construct the necessary devices was a total failure, repeatedly running up against the unanimously unfavourable opinion of all experts, all companies, concerning the design

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of the prosthesis, the potential risks of the procedure, and the medical indication itself. Luck changed when he met three individuals who embraced the idea: two American engineers, Stanton Rowe and Stan Rabinovich, and Martin Leon, the well-known American cardiologist. In 1999, the four founded a start-up (PVT, Percutaneous Valve Technologies, NJ, USA) with the aim of developing a project that everybody else regarded as impossible, dangerous, and unnecessary. A prototype was designed by the ARAN company in Israel, and for more than 2 years, Profs. Alain Cribier and H el ene Eltchaninoff implanted more than 100 prostheses in ovine models as part of acute and chronic studies. Then, on 16 April 2002 in Rouen, they performed together with Christophe Tron the world's first implantation in a 57-year-old man suffering from severe aortic stenosis, in cardiogenic shock and inoperable due to multiple comorbidities. The reaction of the international medical community to this first case defies imagination, even today.

Percutaneous aortic valve implantation has subsequently undergone remarkable scientific evaluation, like few medical innovations before it. As soon as TAVI became commercially available, randomized trials were launched to validate indications based on high levels of evidence and large nationwide registries provided complementary information on real-life use of TAVI. Twenty years after the first human case, TAVI, initially limited to 'compassionate' use in patients with contraindications or high surgical risk, has seen its indications extended by European and American recommendations to intermediate-risk patients and, in 2021, to patients with low surgical risk. More than 3

million patients have now been treated with TAVI, and TAVI has become the reference treatment for patients aged 75 and over with symptomatic aortic stenosis.

The consequences of Alain Cribier's initial discovery and work are not limited to calcified aortic stenosis but also on other valve diseases and have major repercussions in many areas of current cardiological practice, such as the development of imaging technologies and the promotion of multidisciplinary teams and dedicated meetings. He has also inspired countless young doctors to train in these innovative techniques as attested by his major role involvement over the last years in the simulation centre in Rouen.

Despite his international reputation, he remained simple, always accessible, smiling, empathetic, close to his patients, reassuring them, teaching young doctors and his peers, and always supportive of his team. No achievement would have been possible without his exceptional tenacity. Years later, when TAVI was recognized as a breakthrough, we had the opportunity to hear Alain Cribier telling this long quest with simplicity and humour.

The huge international tribute that the news of his death has generated bears witness to his impact on us all. A great doctor has left us, but his work lives on.

## Declarations

## Disclosure of Interest

All authors declare no disclosure of interest for this contribution.