Engineered cardiovascular tissue that grows and deforms similarly as native tissue

Pim Oomen was able to create a ‘stable state’ in engineered cardiovascular tissue, which grows and adapts to the tissue’s mechanical environment the same way as the native tissue it oughts to replace. By creating engineered tissue that can last a lifetime repetitive surgeries for defective heart valves could become something of the past.

Young patients with a defective heart valve often need multiple operations throughout their life since implanted heart valve replacements cannot adapt to body growth and are subject to wear and tear. These repetitive surgeries lead to trauma, financial costs, and increased risk of morbidity and mortality. However, with the development of so-called tissue-engineered replacements, repetitive surgeries may become something of the past. The way these tissue replacements grow and adapt in proportion to the patients body over time determines largely if they will indeed last for a lifetime.

Cardiovascular tissues have the intriguing capacity to actively change their form and function. While these changes are most prominent during embryonic development, most living tissues are in a continuous state of growth and remodeling. Growth (change in tissue amount) and remodeling (change in tissue structure) are of key importance to the functioning of human cardiovascular tissues during both health and disease. Dysfunctional growth and remodeling could for instance lead to aneurysm formation or aortic valve stenosis. Growth and remodeling is also a crucial consideration as we seek to engineer tissue replacements to replace these dysfunctional tissues.

Very few people are aware that the famous scientist Galilei Galileo was the first one to suggest that biological tissues actively change their form and function under the influence of mechanical forces. Now, almost four centuries later, the mechanics of growth and remodeling of biological tissues are still only partially understood. From a biomechanical perspective, it is well accepted that growth and remodeling occur at least partly in response to changes in the tissue’s mechanical environment, in order to maintain a certain stable mechanical state. To date, it has remained unclear what mechanical factor(s) determine(s) this stable state cardiovascular tissues.

By using a wide range of experimental and numerical techniques we found strong evidence that tissue growth and remodeling in human native heart valves occur, from a biomechanical perspective, to maintain a stretch balance. Interestingly, growth and remodeling appear to play opposing roles in maintaining this stretch balance during ageing. At a young age, tissue stretch was decreased by tissue growth and increased by remodeling, whereas at a later age tissue stretch was decreased by remodeling and increased by growth.

To study the mechanics of growth and remodeling in engineered tissues, we designed a bioreactor system in which the mechanics and geometry of engineered tissues could be studied during their development. Using this system, we demonstrated that a stable state could be established in engineered cardiovascular tissues, dependent on their design, in this case scaffold thickness. Evidence of such a stable state in engineered cardiovascular tissues,
similar to the native tissues that they ought to replace, is promising for the field of tissue engineering.