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A multi-scale investigation of biological niches within human calcified aortic valves helps to understand the pathological biomineralization process

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Calcific aortic valve stenosis (CAVS) is the most common form of heart valve disease in the industrialized countries, being an important public health problem [1]. Ectopic calcifications within aortic valve leaflets are strictly associated with CAVS, interfering with cusps opening, they lead to ventricular outflow obstruction [2]. Up to date no proven medical therapy stops CAVS course progression, so valve replacement is the only possible treatment of severe CAVS. Unfortunately, the degenerative valve calcification process, affects also bioprosthetic implants [3]. Being the molecular mechanisms leading to valve calcification still not understood, our aim was to carry on a multi-scale investigation using Scanning Electron Microscopy, Transmission Electron Microscopy and Energy Dispersive X-ray Spectrometry, to provide new insights into calcification process. Severely calcified aortic (tricuspid type, n = 29; bicuspid type, n = 3) and mitral valves (n = 4) were obtained from patients of both sexes (males=25) and different ages (mean age 72±10, range 41-90 years old) undergoing valve replacement due to severe aortic and mitral valve stenosis. We detected bioapatite crystals in two different mineralization sites: niches and extracellular matrix. This suggests the action of two different growth processes: the first occurs in biological niches and it is ascribed to a purely physico-chemical process; the second has the extracellular matrix acting ass the template for a site-directed nanocrystals nucleation. Different shapes of bioapatite crystallization were observed at micrometer scale in each microenvironment but at the nanoscale level crystals appear made up by the same subunits. We suggest that bioapatite nanocrystals in heart valve may activate a strong inflammatory process leading to irreversible pathological condition that, once activated,may aggravate the inflammatory response against bioapatite nanocrystals leading to a severe calcification process.

References

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Keywords
Scanning electron microscopy; aortic valve; calcification.