Annual Report- Zimin Institute for Engineering Solution for Advancing Better Lives

01/2019

Artificial Intelligence Algorithm for Predicting the Optimal Interventional Time for Transcatheter Aortic Valve Replacement

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Brief Summary:

Calcific aortic valve disease (CAVD) is a formation of tissue similar to bone on the leaflets of the aortic valve (AV), which rapidly leads to aortic stenosis (AS). However, patients usually do not have symptoms until the disease has progressed to an advanced stage. Transcatheter Aortic Valve Replacement (TAVR) is a new technology that provides an alternative to open-heart surgical valve replacement. In this type of minimally invasive intervention, a stent with a mounted bioprosthetic valve is delivered through the arterial tree and deployed through the stenotic native valve. Still, there are some doubts regarding the optimal time for intervention in CAVD patients, and concerns regarding TAVR implantation related to complications such as incomplete anchoring, paravalvular leakage, and annular rupture. Our aim is to expand our methods of retrospectively calcification growth evaluation techniques to develop an artificial neural network (ANN) algorithm that will allow us to predict the optimal time for TAVR intervention in CAVD patients and the optimal TAVR device needed to be implanted.

CT scans of pre-TAVR TAV patients were collected from our existing database of CAVD scans. Our Reverse Calcification Technique (RCT) was employed for selected patients in a similar manner to our previously suggested RCT method, to generate various stages of the CAVD disease. This technique is based on using CT scans of calcified AVs to study the calcification progression that leads to the current state. In addition, from each CT scan we extracted additional input parameters: volume & pattern of the calcification deposits for each leaflet and the orifice area of the calcified AV.

The output of the algorithm will result in scoring of the CAVD severity, which will be evaluated according to calculation of the input parameters. The RCT results for each scan will be compared with old CT scans of selected patients in order to relate the CAVD stage with time. This type of information and data will allow us to predict the development of calcification in time, and eventually, the optimal time for TAVR intervention (Figure 1).

Simulations of TAVR deployment inside calcified AV has been performed by our group, towards trained ANN from the simulated biomechanics models. Finite Element (FE) simulations of the deployment of the TAVR devices: Sapien 3, Evolut R and PRO, were modeled inside calcified bicuspid aortic valve (BAV) anatomy (Figure 2). The stents were initially crimped with a cylindrical crimper. The Evolut R deployment is a result of the residual stresses present in the stent after the crimping while gradually pulling the sleeve toward the aorta. The FE solver is SIMULIA Abaqus (Dassault Systèmes, Providence, RI). Computed tomography scan of severely stenotic BAV patient with heavily calcified raphe region was acquired. For this purpose, our existing parametric geometry and mesh generation method was modified for asymmetric BAV, with non-fused cusp angle of 140° and symmetrical fused leaflet. The native leaflets and root were meshed with 3D

elements, and have native hyperelastic tissue properties. The calcium deposits were embedded inside the leaflets and have calcium material properties. The paravalvular leakage (PVL) was also compared using computational fluid dynamics (CFD) models of the diastole in the resulted deployed configurations. FlowVision HPC 3.09 (Capvidia, Leuven, Belgium) was used for the CFD simulations. Similar deployment models will be solved for previous stages of the disease to estimate the desired occasion for intervention.

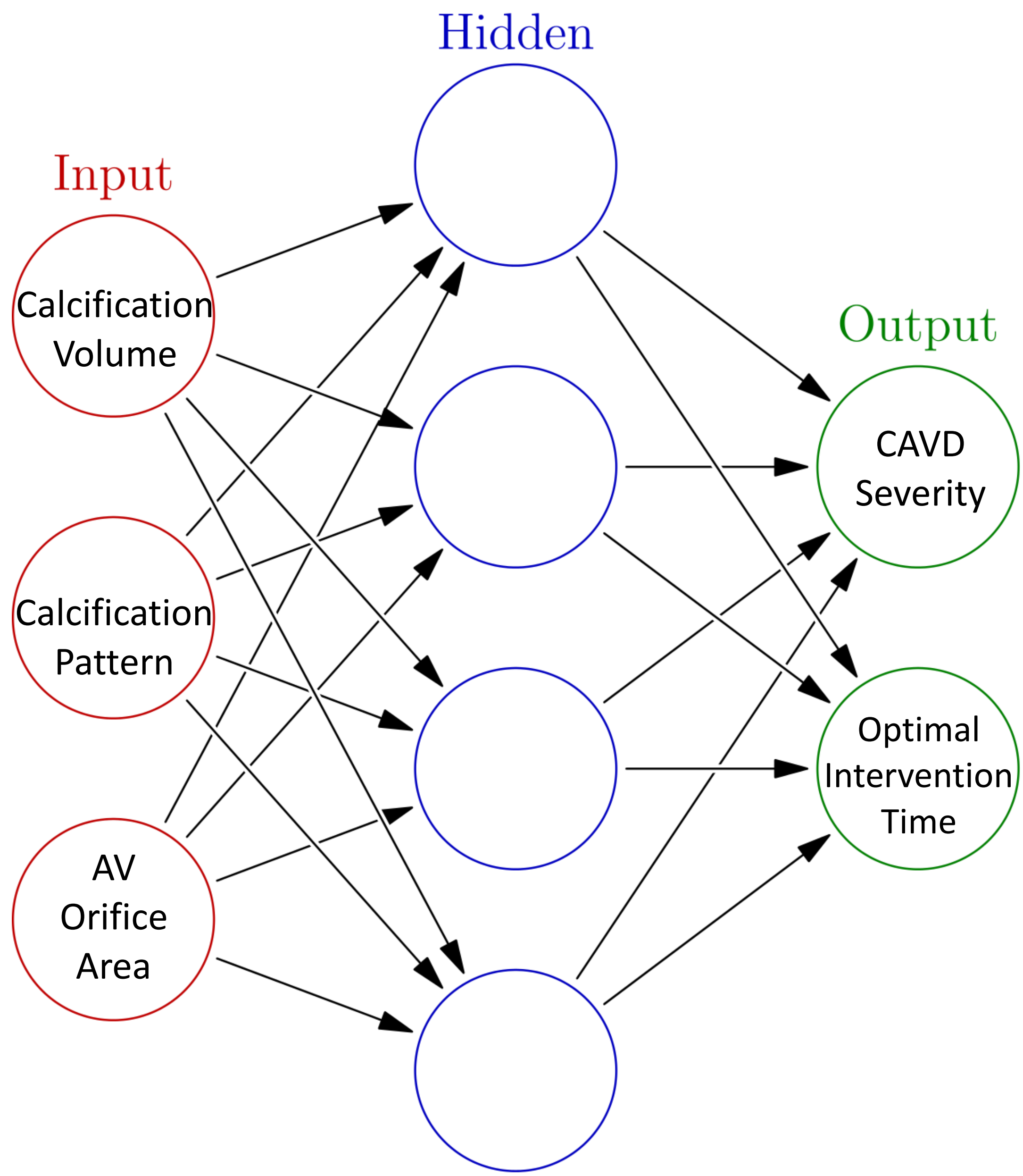
The RCT subtraction algorithm was commenced and used to generate various stages of the CAVD disease in the BAV patient, as seen in Figure 3. An initiation nodule of the calcification growth appears on the raphe region, a location that is subjected to higher stresses in healthy BAV type 1. The non-fused leaflet has similar arc shaped pattern as in TAVs while the arcs are connected in the fused leaflet.

<u>Publications as a result of full or partial Zimin grant</u>:

1. <u>Paper submitted:</u> Lavon K, Marom G, Bianchi M, Halevi R, Hamdan A, Morany A, Raanani E, Bluestein D, Haj-Ali R. "Biomechanical Modeling of Transcatheter Aortic Valve Replacement in a Stenotic Bicuspid Aortic Valve: Deployments and Paravalvular Leakage".

<u>Oral presentations at conferences as a result of full or partial Zimin grant</u>:

1. Morany A, Lavon K, Haj-Ali R. "Integrated Parametric Aortic Valve Models with the LHHM including Pathology and FSI Co-Simulations". Living Heart Human Model (LHHM) annual users meeting, Paris, France April 2018.
2. Morany A, Lavon K, Haj-Ali R. **Webinar**: "Numerical Analysis of Healthy, Diseased, and Prosthetic Aortic Valve within the LHHM. Part 1 - Integrated parametric aortic valve model including pathology and FSI simulations". Living Heart Human Model (LHHM) community, August 2018.
3. Lavon K, Marom G, Bianchi M, Halevi R, Hamdan A, Morany A, Raanani E, Bluestein D, Haj-Ali R. "Biomechanical Modeling of Transcatheter Aortic Valve Replacement in a Stenotic Bicuspid Aortic Valve: Deployments and Paravalvular Leakage". The 8th World Congress of Biomechanics (WCB), Dublin, Ireland, July 8-12, 2018.
4. Lavon K, Marom G, Bianchi M, Halevi R, Hamdan A, Morany A, Raanani E, Bluestein D, Haj-Ali R. "Biomechanical Modeling of Transcatheter Aortic Valve Replacement in a Stenotic Bicuspid Aortic Valve: Deployments and Paravalvular Leakage". Biomedical Engineering Society (BMES) Annual Meeting, Atlanta, Georgia USA, October 17-20, 2018.



<u>Figure 1</u>: Schematic Artificial Neural Network (ANN) diagram illustrating our AI learning modules and algorithms. The overall CAVD pathology is extracted from CT scans of calcified AV we extract the input parameters: volume & pattern of the calcification deposits in each leaflet and the orifice area of the calcified AV. The output of the algorithm will include scoring of the CAVD severity and recommendation for the optimal TAVR intervention time.

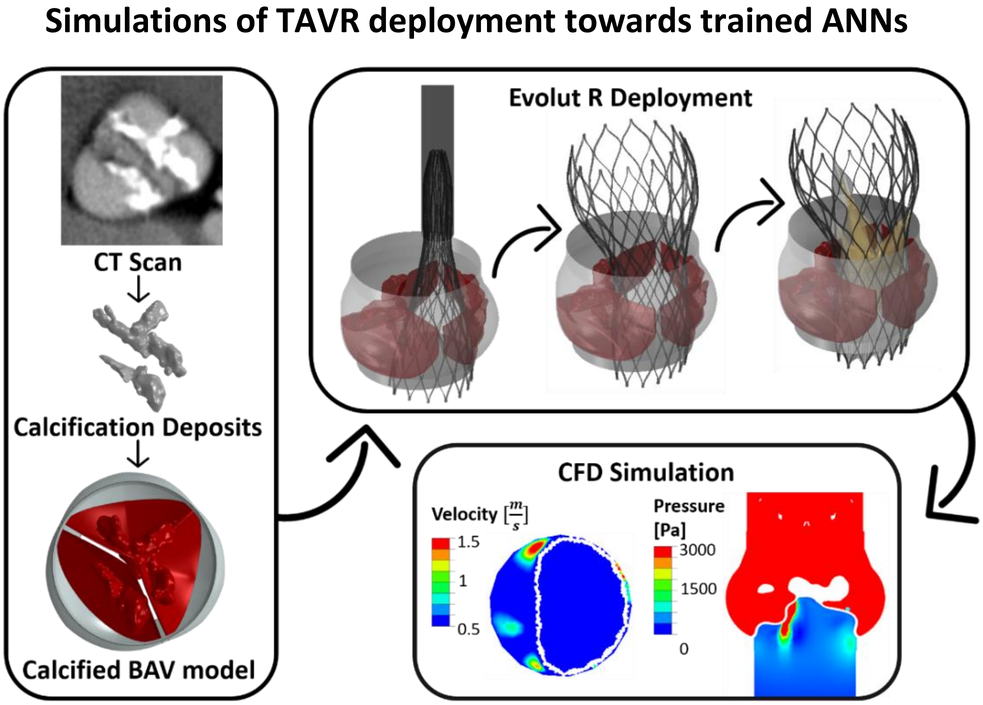


Figure 2: Computed tomography scan of severely stenotic BAV patient was acquired. The 3D calcium deposits were generated and embedded inside a parametric model of the BAV. Deployments of the Evolut R and PRO inside the calcified BAV were simulated. The cuff and closed bio-prosthetic leaflets were added to the deployed stent to obtain the diastolic state. The resulted structural geometry was utilized for computational fluid dynamics simulations to calculate the paravalvular leakage.

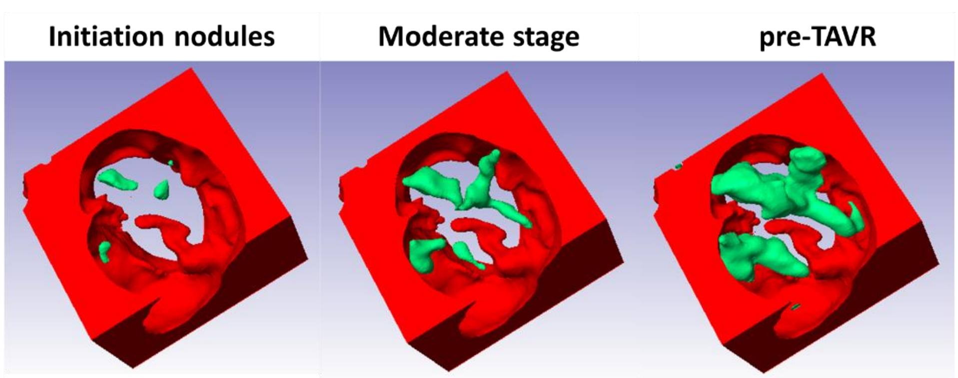


Figure 3: RCT of the calcified BAV patient starting from pre-TAVR CT scan.

Tasks Completed – Year 1:

- Collect and built a new CT-scans database of pre-TAVR TAV patients from Rabin medical center. Those scans include cases of patients with scans from previous years, different calcification patterns and varied stages of the disease. A Helsinki protocol was formulated and approved for the proposed research.
- Programmed and conducted the Reverse Calcification Technique (RCT) on selected sample (n=20) calcified patients.
- Generated new FE simulations of TAVR deployment inside calcified BAV. Those simulations include deployments of the Evolut R, Evolut PRO and Sapien 3 current commercial devices available in the market. In addition, subsequent CFD simulations were also performed to calculate the best suited TAVR (among the three) for each case and quantitate the associated paravalvular leakage.
- ANN structures and training strategies were explored using several open-source and commercial training software.

Tasks Planned for – Year 2:

- Continue collect and built the CT-scans database of pre-TAVR TAV patients from Rabin medical center.
- Continue conducting RCT on larger number of patients (n=50) calcified patients.
- Continue FE and CFD simulations of TAVR deployment inside calcified AV using the Evolut R, Evolut PRO and Sapien 3 available commercial devices. The additional results will allow us to better assess the optimal intervention time and the resulting consequences.
- **Extensive focus will be on:** generating new trained ANN capable of predicting the mechanical and pathological metrics (performance) of the AV given CT-Scans. These will ultimately aid in future medical diagnostics and intervention.
- Analyzing the collected database including measurements of the calcification deposits volumes, orifice area of the calcified AV, in order to determine a mathematical connection between the calculated parameters to the disease stage.
- Analyzing and compare the RCT results with old scans to related the disease development with time.
- Generate several computer simulations of the stages of the disease (based on the resulted RCT), for selected patients with different calcification patterns. Those models will allow us to calculate accurately the severity of the disease.

Zimin group members and responsibilities:

- **Karin Lavon**, PhD candidate – Performing FE simulations of calcified AV and TAVR deployment.
- **Adi Morany**, Msc student – Performing FE simulations of calcified AV and TAVR deployment.
- **Maya Karnibad**, Msc student - Analyzing the CT database and determining mathematical connection between the different measured parameters.
- **Nofar Keizman**, research assistant – Collecting the CT scan database from Rabin Medical center.
- **Shlomo Spitzer**, Msc student –ANN algorithm.

Collaborations:

- **Mirit Sharabi**, PhD, lecturer at Ariel University – joint supervision of Maya Karnibad with Prof. Haj-Ali.

- **Dr. Ashraf Hamdan,** MD - is the director of Cardiovascular Imaging at Rabin Medical Center, Israel. His specialty is in Cardiology and Internal medicine and expertise in cardiovascular CT, MRI, and Nuclear Cardiology.