INTRODUCTION
Calcific aortic valve disease (CAVD) afflicts approximately 0.9% of the Unites States population with 2.8% of people over 75 years of age having moderate to severe aortic stenosis (AS) [1]. The disease is characterized by the formation of tissue similar to bone [2] on the leaflets of the AV, leading to a progressive stiffening (sclerosis) and narrowing of the aortic valve (AV) opening (stenosis). Typical symptoms such as angina and syncope tend to appear at late stage of disease, making a prompt intervention crucial for the patient [3]. Currently, replacement of the valve with a prosthetic valve is the only effective treatment for AS [4].

Transcatheter aortic valve replacement (TAVR) provides a life-saving alternative to open-heart surgical valve replacement for high-risk and inoperable patients [5]. In this type of minimally invasive intervention, a stent with a mounted bioprosthetic valve is delivered through blood vessels and deployed on the stenotic native valve. Currently, the only FDA-approved TAVR devices are the Edwards Lifesciences Sapien and Medtronic Corevalve. These TAVR valves consist of metal stent and bioprosthetic xenograft leaflets. In balloon expandable valves, such as Edwards SAPIEN, the leaflets are sutured to the stent and crimped on the delivery system prior to the procedure. As an alternative, a novel polymeric valve developed by our group [6, 7] is being commercialized by Polynova Cardiovascular, Inc. (Stony Brook, NY) and adapted to TAVR using a self-expanding stent. Polymer TAVR valves could be designed for higher tolerance to damages that may incur during TAVR crimping and deployment. Typical known intra- and postoperative TAVR complications include paravalvular leakage, heart block, thrombosis, embolization or migration of the valve in the left ventricle [8-10].

In recent years, TAVR has been studied using numerical tools and in-vitro tests to find the mechanical stress, hemodynamics and kinematics of the valve [11, 12]. However, these studies focused on the structural mechanics of the TAVR deployment and not on the postoperative conditions or their influence on the hemodynamics.

The objectives of this study are to compare the crimping mechanics of the two valves and to evaluate the effect of different TAVR deployment positions on the patient-specific hemodynamics. First, the crimping mechanics of the Polynova and Edwards SAPIEN were modeled and compared. Then, deployment of Edwards SAPIEN valve in heterogeneous patient specific models was modeled in three axial locations, in order to replicate possible surgical options during the procedure. Lastly, flow models of the deployed valve were carried out in order to determine the optimal deployment location for achieving better patient outcomes based on hemodynamics and the post deployment thrombogenic potential of the TAVR valve.

METHODS
The stents are designed in their expended state based on parametric equations [13] for an estimated crimped position (SolidWorks, DS Corp., Waltham, MA). The materials of the Polynova and SAPIEN stents were super-elastic nitinol and 316L stainless steel, respectively. The Polynova stent incorporated leaflets comprised of xSIBS (Styrene-block-IsoButylene-block-Styrene) material properties derived from our mechanical testing, whereas the SAPIEN stent had bovine pericardium material properties [14]. Hyperelastic material models were used for each study. A hollow cylinder replicated the stent crimpler. Predefined radial displacement of 8 and 9 mm was applied to the inner surface of the crimpler for both novel Polynova and SAPIEN valves, respectively. Precise contact modeling was included to account for the contact among the crimpler, stent and leaflets, and to capture the complex leaflets’ folding. The model was solved in ANSYS Explicit dynamics (Canonsburg, PA).
The CTA scans in systolic phase of two TAVR patients were obtained in the Heart Institute of Stony Brook University Hospital (SBUH) from consented patients, following an IRB protocol approved by Stony Brook University. Automatic 3D segmentation was performed in ITK-SNAP. Region competition snakes approach was employed in order to accurately extract the lumen of the aortic root and the calcifications boundaries. The outer surface of the root was then obtained in MATLAB (Mathworks Inc, Natick, MA) by extruding the lumen surface with a constant thickness for the sinus and a variable-thickness for the AV native leaflets. A solid model was then created in ANSYS Design Modeler (Canonsburg, PA) in which the calcifications were embedded in the soft tissue.

Combining the two models, an implicit finite element analysis of the TAVR procedure was performed, in which the location of the TAVR valve with respect to the AV annulus was parameterized, to replicate different choice of the surgeon during the deployment (Figure 1). The native leaflets soft tissue was modeled with an anisotropic hyperelastic material calibrated with tensile-test experimental data on excised human AV leaflets, obtained from the SBUH tissue bank. The calcium material model was calibrated performing nano-indentation measurements after µCT-scanning the calcified part of the same AV leaflets specimens. Computational Fluid Dynamics (CFD) analyses were performed for the optimal deployed configurations, to estimate the paravalvular leakage volume in diastolic phase.

RESULTS
The maximum stress levels in the crimped valves and stents (both the absolute level, and the stress level normalized with respect to the ultimate yield stress of the corresponding materials) were higher for the SAPIEN valve (Figure 2). The normalized value of the peak von Mises stress magnitudes to the ultimate stress levels are 9.1% and 24.7% for the novel Polynova and SAPIEN valve respectively. The maximum stresses in the leaflets were observed in the subcommissural triangles of the native leaflets bonding with the struts in both valves. The minimum stresses for both valves were observed at the belly region of the leaflets. The peak stress magnitude of the stent alone in its crimped state was also higher in SAPIEN than in Polynova. The highest stress levels of Polynova stents were observed in the aortic side of struts where buckling occurs whereas for SAPIEN valve the highest stresses were observed on the strut joints.

Anchorage of the valve was assessed for three different axial configurations: 70% toward the aortic side, 70% toward the ventricular side and midway (Figure 1). Stresses within the wall and interaction of calcium-soft tissue were investigated during the deployment. Higher stress levels were found in the calcium deposits than in the soft tissue (Figure 3). For both patients, who experienced valve migration during the procedure, incomplete expansion of the valve occurred and paravalvular leakage was confirmed in the correspondent CFD simulations. The risk-minimizing deployment configuration was assessed for both patients.

DISCUSSION
This study compared two TAVR valves and three deployment locations based on the crimping stresses and the deployed valves hemodynamics, respectively. The stress magnitude in the crimped configurations of Polynova and SAPIEN leaflets had small differences. However, the much lower stresses in the crimped state strongly indicate that the polymer valve may withstand damage much better than the tissue valve. Accurate patient-specific AR models including the vessel wall thickness and calcification deposits represent a useful tool to guide TAVR and to help in preventing the migration of the valve during the deployment procedure. Additionally, optimizing the positioning of the valve during deployment, as well as alternative approaches to TAVR valves tailored to patient’s specific pathology, e.g. polymeric valves, may offer better procedural outcome. Ongoing studies in the CFD models include calculation of thrombogenic footprints based on stress accumulations along platelets trajectories. These models are validated with in vitro hemodynamics and their thrombogenicity correlated by measuring platelet activity using our platelet activity state (PAS) assay.

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REFERENCES