Discussion to: Bioinspired Polymeric Heart Valves: A Combined In Vitro and In Silico Approach

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Dr. Toshiharu Shinoka (Columbus, OH):

So, I would like to thank the AATS, Dr. Kim, Dr. Carr, for the opportunity to discuss this paper today. Congratulations, Dr. Lee and colleague, for your exciting and unique attempt to create a polymeric heart valve using computer-aided design software, mimicking the native [polymeric?] valve. After production of the prototype, you also tested its valvular performance, both computationally and experimentally, using a pulse duplicator. I would also like to thank Dr. Lee for providing me with your manuscript well in advance. I have several questions. The first question is regarding the material choice. Could you briefly explain why you chose this material and these concentrations? And did you have any chance to compare other polymer materials in the same pulse duplicator?

Dr. Aeryne Lee (Sydney, Australia):

Yeah. So, thank you so much for the comment and for the questions. I believe the first part of the question was regarding the choice of material and the
concentrations. So, I'd like to address two parts of this. The first one is the valve mold material. We used a polypropylene material, and there was sort of two main reasons for this. The first one was that the polypropylene material does not dissolve in the solvent that was used for the polymer for the valve, which is obviously very important. The second sort of reason is because polypropylene is a material that can quite easily and quickly be 3D printed. What this meant for us in developing this workflow meant that we could quite efficiently work through and progress all the way from design to fabrication to testing by using this material. In terms of the valve material, we used a siloxane-based polyurethane because of its very favorable biostability, biocompatibility, and bioinertness, as well as its mechanical properties. It's actually quite difficult to find a polymer that can balance these two factors well. The second reason is because it's a material that is actually compatible with the dip coating process. So not all polymers can be processed in the same way. In terms of concentrations, which is not actually something I addressed in the presentation but in the manuscript, we used concentrations of 11 to 15 weight/volume percent for the select siloxane-based polyurethane. And this was a little bit of trial and error, but the reason was because with these concentrations, we could actually achieve the thickness that we wanted, which was about 100 to 200 microns for the leaflets. And another similar reason was that this concentration was appropriate for the dip coating process. We ended up with a polymer solution that was not too viscous nor too runny. So those are the reasons behind the material choice. Thank you.

Dr. Shinoka:

So, my next question is why the thinner valve leaflet had a higher regurgitation fraction. I think it is easy to understand that the valve with a thinner leaflet had a larger EOA. I thought that the thinner valve might have a better coaptation with lower regurgitation. Do you have a comment?

Dr. Lee:

Yes. So that is a very good point, actually. And I wanted to start off by mentioning that, potentially, the relationship between regurgitant fraction and leaflet thickness may not necessarily be linear. And so, for, say, the thinnest possible valves versus the thickest possible ones, potentially out of the range that we tested for this work, we could find a thickness of leaflets that is actually optimal for getting the favorable EOA and regurgitant fraction. That being said, we believe that there may be two possible reasons why we saw this sort of, let's say, trend with finding the thinner leaflets had a higher regurgitant fraction. The first reason may be that the leaflets were just so thin that perhaps they were not able to withstand the backwards pressure as well as the slightly thicker leaflets. That might be one of the reasons. The second reason could be that, as you mentioned, because the thinner leaflets had a greater EOA, we would actually expect them to open more. And so, in order for them to go back into the closed position it may require more time, and they have to also travel more distance before they can reach that closed position. And so, we believe that, potentially,
there was a higher closing volume. And because regurgitant fraction is obviously a combination of closing volume and leakage volume, that might actually be where we were getting the increased regurgitant fraction.

Dr. Shinoka:

Okay. Thank you.

Dr. Lee:

Thank you.

Dr. Shinoka:

So, my final question is regarding the calcification issues. In the long-term period, do you have any plan to implant this valve in the sheep model or animal model? Which is the best model to check the calcification of the valve leaflet? After the prototype was tested in vitro, I think your next step would be an in vivo testing before translating to the clinical setting.

Dr. Lee:

Yes, definitely. So, we endeavor to actually implant our polymeric valves into sheep models to, as you mentioned, assess the calcification and also assess sort of the behavior and durability of the valve in the natural environment. So yes, it is definitely actually the next step, once we've established all of the in vitro studies that are necessary for assessing the valve.

Dr. Shinoka:

Okay.

Dr. Lee:

Thank you so much.

Dr. Shinoka:

Thank you. Congratulations.
Dr. Lee:

Thank you. Thank you.

Dr. Bill DeCampli (Orlando, FL):

Hi. Bill DeCampli. So, I know you're an engineer, so I thought I’d ask just a few naive engineering questions. So, I have a little familiarity with the dip coating process. So, every detail counts as to how these leaflets are made. So how in the drying process do you guarantee you have uniform thickness over the surface area of the leaflet?

Dr. Lee:

Yeah. That is a very great question. And it's actually something that is, I would say, probably one of the most challenging things when it comes to fabrication, especially via dip coating. And it is something that we are working towards trying to achieve. As I mentioned before in my talk, we were having a bit of difficulty trying to achieve constant thickness throughout the leaflets for the dip coating process. At the moment, a lot of the things are done quite manually, but we are working towards fully automating this process to, hopefully, enable a more constant and reproducible sort of method, so.

Dr. DeCampli:

Yeah. And then the final question should be brief. But I'm just guessing that, because your computational model involved fluid-structure interaction, that can be pretty complicated and computer-demanding. Did you assume zero viscosity for the fluid, or--?

Dr. Lee:

Yeah. Correct. So, this model actually has inviscid fluid. So, we're not actually taking into consideration the viscosity just yet, but that is actually the next step of our modeling team. We're trying to involve that sort of viscous effect onto the structures.

Dr. DeCampli:

Okay. Good.

Dr. Lee:
Thank you so much.

Dr. DeCampli:

All right. Great presentation.

Dr. Lee:

Thank you so much.

Unidentified Speaker 1:

Very good answer. And actually, I can tell you from my own experience, even after automation of the process, still controlling the thickness of these leaflets with dip molding is extremely difficult.

Dr. Lee:

Yes. Thank you.