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Protecting the Pregnant Occupant: Dynamic Material Properties of the Placenta

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ABSTRACT

Automobile crashes are the largest cause of death for pregnant females and the leading cause of traumatic fetal injury mortality in the United States. Computational models, a useful tool to evaluate the risk of fetal loss in motor vehicle crashes, are limited to quasi-static material properties of the placenta. This study presents a total of 8 dynamic uniaxial tension tests on the full thickness of the placenta and 8 dynamic uniaxial tension tests on the maternal side of the placenta. These tests were completed from 4 human placentas to determine material properties at a strain rate of 6 strains/s. The results show that the average peak strain at failure for both the maternal portion and the full thickness placenta are similar with a value of 0.36. However, the peak stress for the full thickness placenta, 119.4 kPa, is much higher than the peak stress for the placenta with the chorionic plate removed, 27.5 kPa. These results are compared to previous quasi-static data and found to be significantly different ($p<0.01$). In summary, dynamic loading data for the placenta have been determined for use in computational modeling of pregnant occupant kinematics in motor vehicle crashes. Moreover, for predicting placental abruption, the computational model for the maternal side of the placenta should reflect the material properties for the villus structure of the placenta.

INTRODUCTION

Automobile crashes are the largest cause of death for pregnant females and the leading cause of traumatic fetal injury mortality in the United States (US) (Attico et al., 1986; Weiss et al., 2002). Each year in the US, 800 to 2800 fetuses are killed from motor vehicle crashes (Klinich et al., 1999a; Klinich et al., 1999b; Pearlman, 1997; Pearlman et al., 1996; Weiss, 2001). The best way to protect the fetus is to protect the mother considering that maternal death has a near 100% fetal loss rate (Pearlman et al., 1990a). If the mother survives, protection of the fetus may best be accomplished by preventing placental abruption. Placental abruption, which is the premature separation of the placenta from the uterus, has been shown to account for 50% to 70% of fetal losses in motor vehicle crashes (Pearlman et al., 1990b).

Computational modeling of the pregnant occupant kinematics provides the widest basis for studying factors that could prevent adverse fetal outcome from a motor vehicle crash (Moorcroft et al., 2003a; Moorcroft et al., 2004; Moorcroft et al., 2003b; Moorcroft et al., 2003c). However, material parameters for computational modeling come from early research on placenta tissue at quasi-static loading rates (Moorcroft et al., 2003a). Because abdominal loading in an automobile crash is at a dynamic rate, the placenta tissue material properties should be evaluated with a dynamic loading condition.

The microstructure of the human placenta is important in modeling the material response to dynamic tension loading. The human placenta connects to the uterine wall, usually in the fundus of the uterus, and provides a means for the maternal-fetal exchange of gases and nutrients (Ramsey, 1975). However, because of the different roles it serves for the mother and fetus, there are microstructure differences on the maternal and fetal sides of the placenta (Figure 1) (Cunningham et al., 2005). The fetal side of the placenta includes the chorionic plate. This layer of the placenta is filled with fetal blood vessels that originate at the umbilical cord and radiate outward to the edge of the placenta in a dense network. The maternal side of the placenta is a network of villi and intervillus spaces. The purpose of this study is to test two placental tissue groups in uniaxial tension at dynamic loading rates. The study quantifies the loading and failure material properties of the full thickness placenta as well as just the maternal side of the placenta.

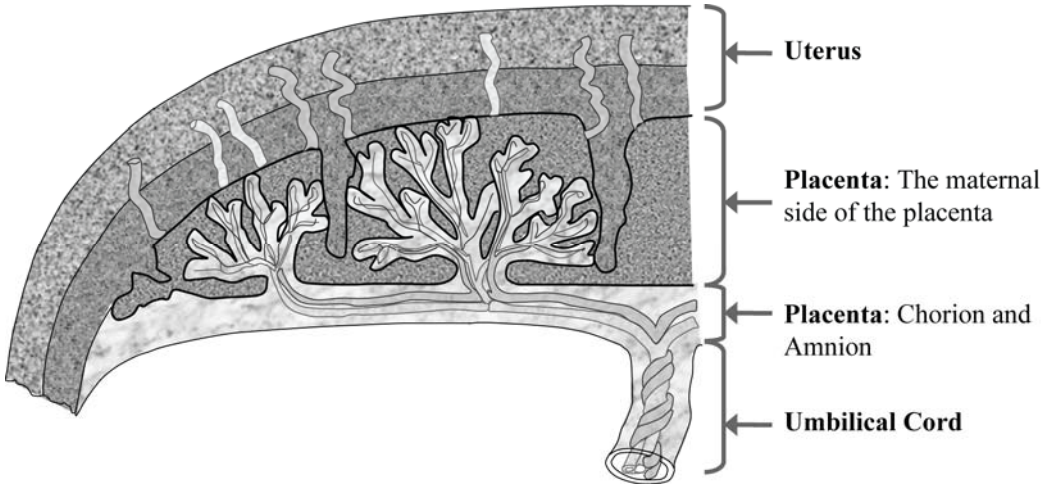

Figure 1: The structure of the placenta varies from the maternal to the fetal side.

METHODS

This test series utilized four whole human placentas. Donor tissue followed the Wake Forest University Baptist Medical Center institutional review board informed consent procedures. All tissues were kept fresh, in saline, and tested within 7 days of delivery. A total of 16 specimens were extracted from 4 whole placentas. While 8 specimens included all layers of the placental tissue, 8 additional specimens had the chorionic plate removed. The latter specimens allowed for testing of only the maternal portion of the placenta.

A high-rate servo-hydraulic Material Testing System (MTS) was used for uniaxial placental tissue dynamic tension tests. The tissue was held in place by a set of cryogenic grips with a preload of 1 g. The steps for this process are discussed in detail in Manoogian et al. (2007). Instrumentation for the tests included a load cell (OMEGA LCHD, 25 lbf, Stamford, CT) and accelerometer (Endevco 7264B, 2000 G, San Juan Capistrano, CA) to measure the reaction load and compensate for the inertial loading above the load cell (Figure 2). The MTS displacement transducer recorded global displacement. The MTS piston moved at 0.5 m/s which corresponded to a strain rate of 6 strains/s. A high-speed video camera (Phantom V4, Wayne, NJ) recorded the test event at 1000 frames per second with 512 by 512 resolution.

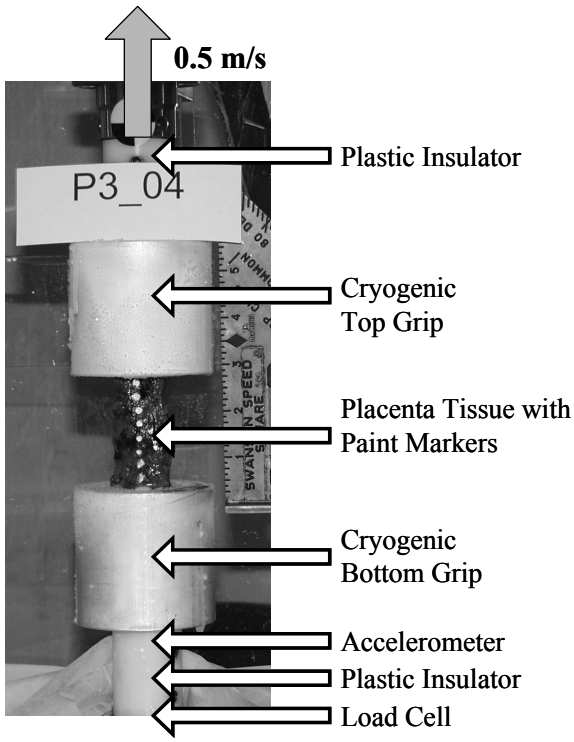

Figure 2: The high rate MTS pulled the tissue in tension to failure at a rate of 0.5m/s. Instrumentation recorded the load and displacement to report stress and strain curves.

True stress and green-lagrangian strain curves were calculated for each specimen. Paired t-tests were used to test for significant differences between the full thickness placenta and the maternal side of the placenta for peak strain and stress. Standard deviations of the stress and strain values were also calculated for each group of specimens.

RESULTS

Stress versus strain curves for the full thickness placenta and the maternal side only are presented for dynamic tension tests. All of the data are plotted together for the full thickness placenta with the average and standard deviation for the stress at each strain (Figure 3). The average peak stress for the full thickness placenta was 119.4 ± 27.6 kPa. The corresponding peak strain was 0.36 ± 0.04. All of the stress-strain data are plotted together for the maternal side of the placenta with the average and standard deviation for the stress at each strain (Figure 4). The peak strain, 0.36 ± 0.09, was similar to the full thickness placenta group. However, the peak stress in the maternal side only group was 27.5 ± 14.2 kPa.

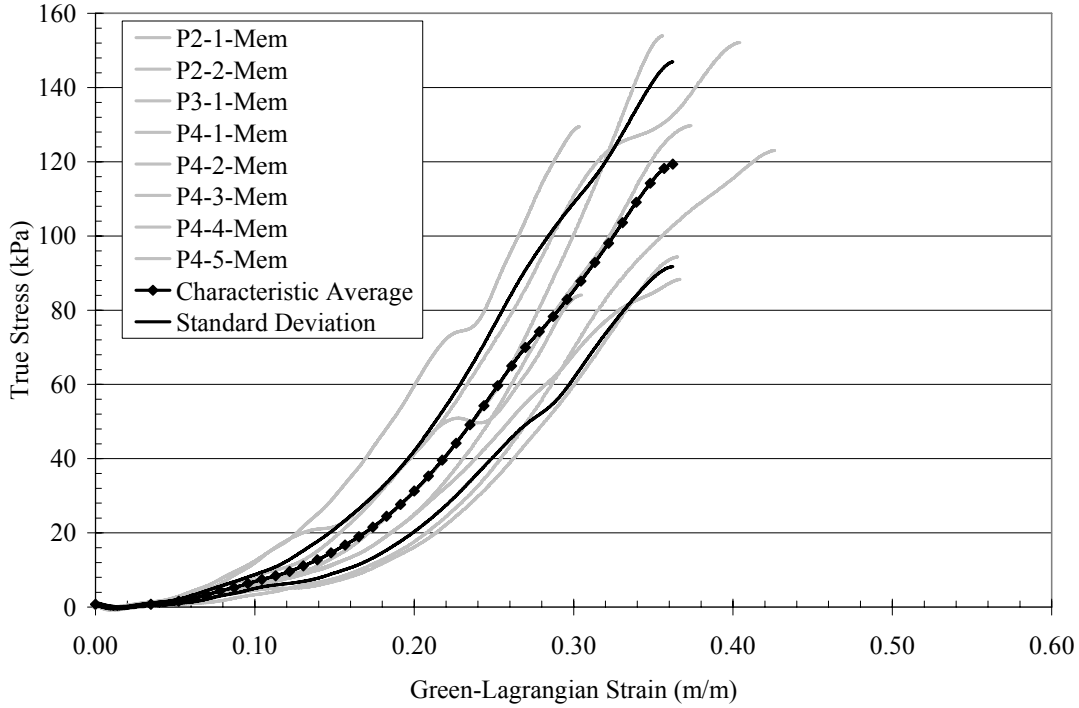

Figure 3: All of the tests for the full thickness of the placenta have similar stress versus strain curves.

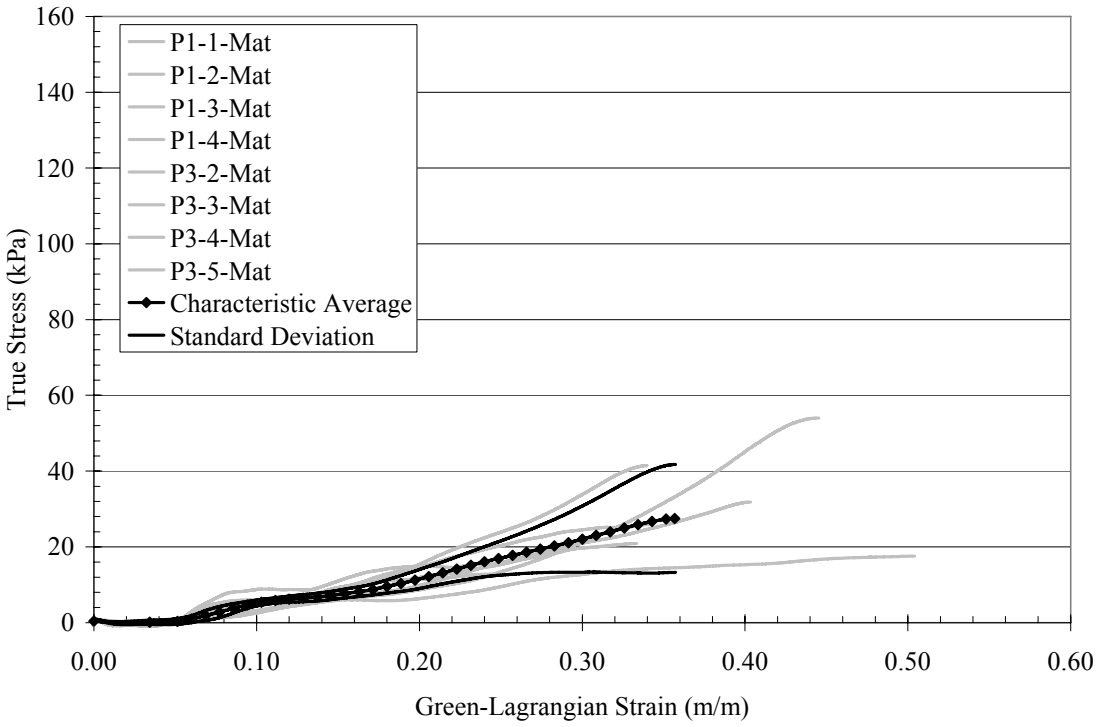

Figure 4: All of the tests for the maternal side of the placenta have similar stress versus strain curves.

The characteristic averages show the entire thickness of the placenta provides a stiffer response than the maternal portion alone (Figure 5). T-tests evaluated the peak stresses, peak strains, and moduli for the dynamic placenta and dynamic placenta with the chorion removed. The stresses are significantly different ($p<0.001$) for the two groups of placental tissue but the peak strains are not ($p=0.9$). The average elastic modulus in the linear region is also significantly lower for the maternal side of the placenta than for the full thickness placenta ($p<0.001$).

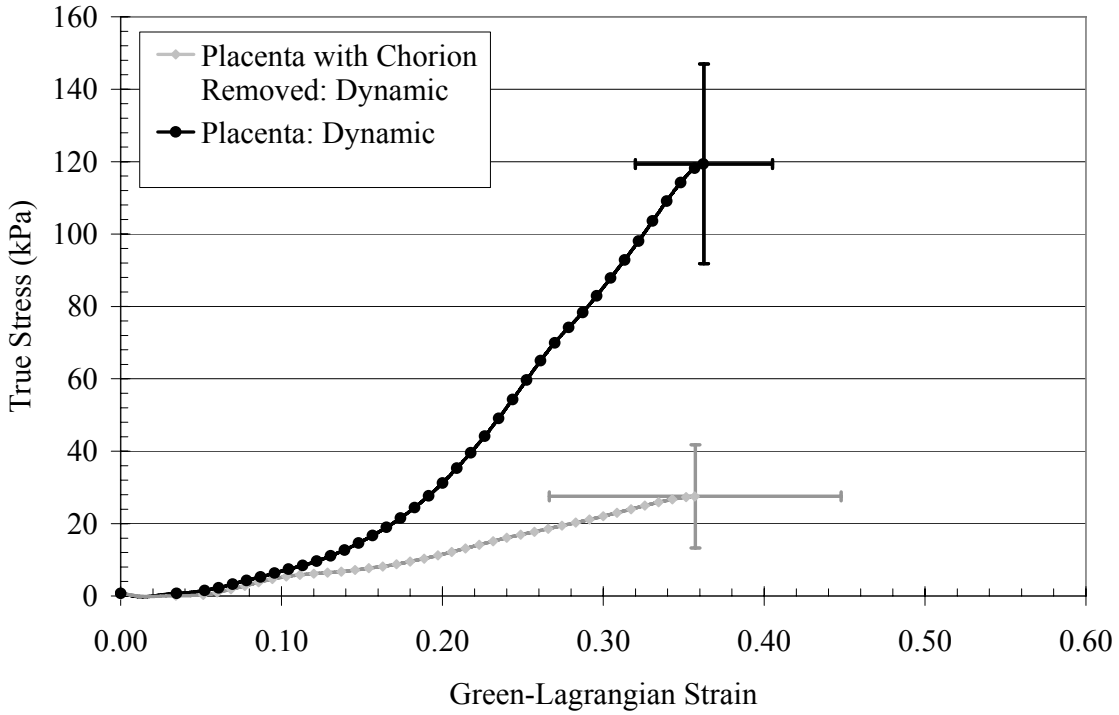

Figure 5: The averages show the dynamic placenta is stiffer than the maternal portion of the placenta. The standard deviations of the peak values are indicated with bars.

DISCUSSION

The results from this study give respective stress-strain curve loading and failure information for the full thickness placenta and the maternal side only of the placenta. The full thickness placenta specimens include the chorionic plate. As a result, the elastic modulus and failure stresses are much higher when this dense layer of blood vessels is present. The maternal portion of the placenta, including only the villus structure, has a more compliant stress-strain response and therefore has a lower failure stress and elastic modulus than the full thickness specimens. Both the maternal side of the placenta by itself and the full thickness placenta have similar failure strains. The standard deviation in the failure values is assumed to be dependent on specimen variability since the testing procedure was the same for each specimen.

These dynamic testing data are compared to previous quasi-static placenta tension research (Pearlman, 1999). While, the quasi-static tests are sub-failure and the tests in this study are failure, this is the most suitable previous research for comparison. It is assumed Pearlman's tests were completed on the full placenta with the chorionic plate attached since it is not documented. When compared to the full thickness dynamic tests the peak stress, peak strain, and linear modulus were all significantly different ($p<0.01$). The p-values from paired t-tests also indicate significant differences in the peak strain and linear modulus between the dynamic loading of the maternal portion of the placenta and quasi-static loading of the full thickness placenta ($p<0.01$). However, the peak stresses for these two test series were not significantly different ($p=0.08$). For dynamic testing of the same viscoelastic tissue it is expected that the peak strain is reduced and the peak stress and elastic modulus are both increased (Yamada, 1970). The results from this study compared to testing by Pearlman (1999) agree with this viscoelastic theory.

Moreover, for dynamic testing of placental tissue, implementing and adapting a cryogenic grip mechanism provided necessary advantages. One advantage of this method was the ability to grip the tissue throughout the thickness. This ensured the internal layers strained the same amount as the external layers, which is important in quantifying the failure stress and strain of the material. Another advantage of the cryogenic grip was it eliminated potential slipping of the tissue in the grip during the dynamic test. In addition to these advantages, there are limitations with this study. It is assumed that since the placenta tissue maintains its size and shape after delivery, the tests postpartum provide a close model to the performance of the tissue *in situ*. Additionally, an increase in the sample size would allow various dynamic rates to be tested. In this study, only a single dynamic rate was tested. For each specimen, global displacement was used for calculating strain until failure. This provides a slight underestimate of the local strain at the failure location (Manoogian et al., 2007).

CONCLUSIONS

This study presents a total of 8 dynamic uniaxial tension tests on the full thickness of the placenta and 8 dynamic uniaxial tension tests on the maternal side of the placenta. These tests were completed from 4 human placentas to determine material properties at a strain rate of 6 strains/s. The results show that the average peak strain at failure for both the maternal portion and the full thickness placenta are similar with a value of 0.36. However, the average peak stress for the full thickness placenta, 119.4 kPa, is much higher than the average peak stress for the placenta with the chorionic plate removed, 27.5 kPa. This is due to differences in the structure and function of these layers in the placenta. In summary, dynamic loading data for the placenta have been determined for use in computational modeling of pregnant occupant kinematics in motor vehicle crashes. Moreover, for predicting placental abruption, the computational model for the maternal side of the placenta should reflect the material properties for the villus structure of the placenta.

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DISCUSSION

PAPER: **Protecting the Pregnant Occupant: Dynamic Material Properties of Uterus and Placenta**

PRESENTER: ***Sarah Manoogian, Virginia Tech – Wake Forest Center for Injury Biomechanics***

QUESTION: *Guy Nusholtz, DaimlerChrysler*
It looked like, in your tests, that you had a lot of variation when you were doing uniaxial tests, and I don't know how you would get an accurate measurement of the actual strain to failure type of properties because locally where it's going to strain, where it's going to fail, you're going to have a bit more strain. And with that in mind, it looked like you had an awful lot of scatter in your data. So you may not have a difference between the x and y results that you've demonstrated. That could just be an artifact of the variation that's occurring in the test procedure. Could you comment on that?

ANSWER: Well, I think that was a 2-part question. The first question was uniaxial and the second was biaxial?

Q: Yes.

A: Okay.

Q: The first part was noticing in the uniaxial that you have the potential for a lot of variation and noticing in the biaxial, you also had that. So how do you know that your differences are really differences?

A: Well, they're very different tests. In the uniaxial test, we measured the strain using the global piston displacement and we do have variation in those specimens, but I don't—I'm trying to remember what your question was regarding that. You're saying there's a lot of variation here?

Q: Yes, if you go back and look at those tests. Go back to that one. Okay. You've got a reasonable amount of variation. No, go to the other one. Okay. You've got a reasonable amount of variation. Then when you go to the biaxial test, you've also got a reasonable amount of variation.

A: Right. Well, the variation here—I mean, we're getting four different human placentas. Those are all from four different mothers with different gestational experiences and, you know, there are several things that contribute to the placental development: smoking, exercising a lot or overweight. I mean all these things affect your placental development. So we're not saying that all placentas are the same. What we're doing is showing, based on specimens from various placentas, this is the average characteristic. And I think that this is a very good sample of that.

Q: But part of your variation could be the way you're estimating the strain.

A: We're not estimating strain here. We're measuring strain using the piston displacement. And we looked at the optimal markers to look at the actual element that failed, and we determined that that was not a good measure based on just this porous tissue elongating. So we have a very consistent measurement of strain for these tests.

Q: Yes. That's a global measure, then, when you're just looking at the piston.

A: Right.

Q: So you're not looking at the strains at different places.

A: Right. Well, I do have that. You know, if we took one test—That was the video that doesn't like to play. If we looked at one test and we tracked optimal markers, you do have some elements that strain a lot more than other elements. But in order—If you look at the average distribution over the tissue, it's very similar to the average—to the measurement of piston displacement. So if you average all these elements, some are straining more and some are straining less, but the average is represented by that piston displacement. So I think that this is a very consistent way of measuring the strain for these uniaxial tests.

Q: Okay. That's fine, but the point is that the local strain, which is going to predict the failure—

A: Right.

Q: Is going to be all over the place.

A: There is some variation in the local strain that we are not able to account for.

Q: And then when you go to the biaxial and you've got those two curves, they may not be different and that could be due either to experimental—

A: This could be due to the experimental setup. This could be—

Q: Right.

A: Due to different gestations, but what we're just looking at is an average representation of a dynamic loading event for the pregnant uterus.

Q: Okay. Thank you.

Q: *Stephen Ridella, NHTSA*
It's nice to see us moving forward, Sarah. How do the properties you derive in this current study do with the current models?

A: Right. Well, the current model that we use at Virginia Tech is based on previous quasi-static testing of tissue and some of those are non-pregnant uterine specimens and some of those are specimens that have been frozen and these are not. They're very similar in their values, but I can't, off the top of my head, say the stress is higher or lower, but this will advance those, as far as having the full stress/strain curve and just a failure value.

Q: It'll be interesting to see how these come out in future models. Thanks.

A: Okay. Thanks.

Q: *Jeff Crandall, UVA*
Nice study. I had a comment on using the averages here for the x and y values. In actuality, you've got a paired comparison between an x response and a y response for a given piece of tissue. When you take the averages that may not fit any particular tissue. So what you might want to do is use the finite element you've talked about and use that to determine, simultaneously, all the parameters.

A: Right.

Q: So, because this is—Normally, a lot of people don't do constitutive models for this reason on an anisotropic material because you don't really know how to average the responses.

A: Right.

Q: *Richard Kent, University of Virginia*
You have a 40-45% failure strain in these biaxial tests. And in the axial, did I see it correctly? It's quite a bit lower. About 25%?

A: The uniaxial tests are the placenta and this is the uterus.

Q: Oh, okay.

A: But yes, the placenta is lower. Theoretically if we did uniaxial tests, that strain should be higher for the same tissue because you're not restricting motion in the other direction, but that's a separate tissue that has a separate peak strain.

Q: And on the uniaxial tests, are you also using the generalized Lagrangian strain or are you just using change in length-per-length?

A: No, we're using the true stress values. We're actually looking—

Q: Talking about strain.

A: We're actually using the true values for both of those. We're looking at the change from the step before that.

Q: Yeah, but there's a—So you're saying it's an Eulerian measure of strain that you're using? You're using the current length to divide by, not the initial length?

A: Right.

Q: Okay, but you'd still have—You have a geometric non-linearity so the strain sensor that you showed for the biaxial test is a generalized Lagrangian strain tensor so that has, as its basis, the undeformed shape. And so I'm wondering in the uniaxial tests, are you also using that generalized description of strain or are you just using change in length?

A: No. We're just looking at the change in length.

Q: So there's a geometric non-linearity you're missing in that test. If you're pulling to 25%, your error in strain is probably about 25% if you don't have that generalized description of Lagrangian strain that you're using in the biaxial test. So you might want to check to make sure you're using a consistent measure of strain.

A: I do believe we're using a consistent measure. I think some of our communication is—

Q: I mean—So are you using, you know, the F transpose F minus one? Are you using that for the uniaxial test as well?

A: No.

Q: Okay. So there's a geometric non-linearity that's missing in the uniaxial test. I'm just saying.

A: Okay. Maybe I can talk to you later about how to decipher that.

Q: Okay. The other one quick question: Have you looked at this as a function of a sort of developmental course? I know it should change quite a bit as you get closer to delivery, right?

A: Right. We would love to do that if we had more available tissue. Unfortunately, you can't really get the placenta until after delivery. And so, this is just assumed at full gestation when that connection would be most delicate.

Q: Got you. Okay. Good work. Thank you.

Q: *Barry Meyers, Duke University*
So I won't pick on your mechanics. The thing I'm curious about: You have a vascular, highly vascular tissue in the placenta and then a smooth muscle dominated tissue in the uterus. And in one case, you're looking at it unpressurized and in the other case, the cells are dead. So I wonder what your thoughts are on where those curves might go if you were actually able—and I realize you wouldn't do this in this study, but if you were actually able to pressurize the placenta in this study and you were actually able to deal with at least viable cellular structures in the uterine wall.

A: Right. I mean, that's something that we don't know because we haven't done tests on that. We would like to do that in the future. Obviously these are very different than how the structures are in vivo. The placenta is much thicker in vivo because it's so fluid-filled and it's lost a lot of that blood by the time we've tested it, and we're just not really able to look at the in vivo properties of these tissues and how that affects your material structure—their material properties.

Q: It might be worth, before doing more testing, to actually spend some time and consider what the impact of those kinds of physiologic events are on where these curves might be because I'm guessing some of these could be a factor of two or even order magnitude changes.

A: Right. We were just trying to, you know, get the first step in advancing the pregnant models by going to a dynamic, non-linear, stress/strain curve based on the previous quasi-static linear curves.

Q: Understood. Thanks.

A: Thank you.