Inverse Relationship between Local Wall Shear Stress and Plaque Thickness in Coronary Arteries is Retained by Compensatory Enlargement in Early Atherosclerosis

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Abstract

Background: In coronary arteries, it is hypothesized that areas of low wall shear stress (WSS) are associated with increasing plaque thickness (PT) during atherosclerotic progression. This dynamic relationship cannot be observed directly, since obstructive plaque development affects WSS distribution. Therefore, we investigated if this relationship could be seen in areas of compensatory enlargement (outward remodeling) without luminal narrowing, thus representing the pre-disease WSS. We determined the point of atherosclerotic disease progression at which the inverse relationship diminishes.

Methods: 48 in-vivo intravascular-ultrasound (IVUS) pullbacks (21 LAD, 9 LCX, 18 RCA) from 29 male and 11 female patients were reconstructed by geometrically correct 3-D fusion with X-ray angiography, and computational fluid dynamics methods were employed. After excluding branches, calcified and stented regions, a total of 3,918 cross sections were automatically analyzed; of these, 1,947 were within the 10-40% area-stenosis range (plaque+media area over vessel area) associated with compensatory enlargement. WSS and PT were calculated at 72 circumferential locations within each cross section, and for each location the existence of an inverse WSS/PT relationship was assessed.

Results: In 31 of 48 vessels, at least 35% of the cross sections were in the compensatory-enlargement range. In 19 of those vessels (61%), inverse WSS/PT relationships were observed significantly more frequently in the segments within the compensatory-enlargement range than in the vessel as a whole ($p<0.025$). When also including the 17 vessels with less than 35% of the cross sections within the compensatory-enlargement range, a statistical difference in inverse-relationship presence was no longer observed ($p>0.75$).

Conclusions: The inverse relationship between WSS and PT is significantly more pronounced in vessel cross sections within the compensatory-enlargement range as compared to the full spectrum of vessel stenosis severity. If less than 35% of a vessel segment remains without luminal narrowing, thus advanced atherosclerosis, the strength of this inverse relationship diminishes and is no longer significant.

(numbers have been updated by additional patient data since abstract submission)

Disclosures

None of the authors has indicated any conflict of interest. This study was approved by the Human Subject Offices of both institutions involved.

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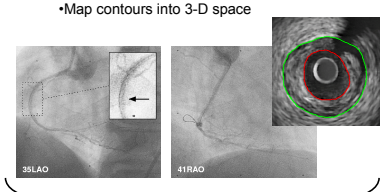
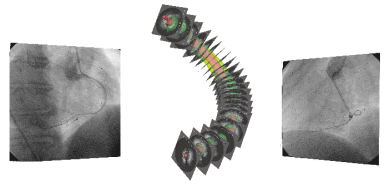
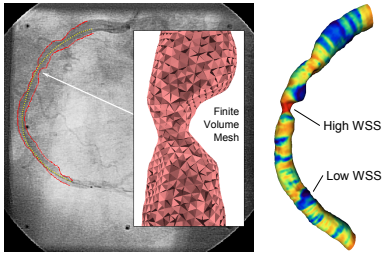
Modeling

- All subjects had clinically indicated catheterization.
- An accurate three-dimensional model of the vessel under consideration is needed.
- Biplane X-ray angiography or a pair of single-plane angiograms provide geometric information.
- Intravascular ultrasound (IVUS) pullbacks provide cross-sectional information.
- Fusion yields the 3-D model of the vessel:
  - IVUS path and vessel lumen from angiography
  - Lumen and media contours from IVUS data
  - Map contours into 3-D space



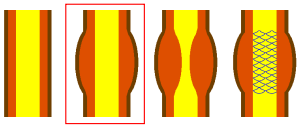


- The 3-D model is utilized to measure plaque thickness and local hemodynamics.
- Computational fluid dynamics (CFD) methods yield wall shear stress distribution:



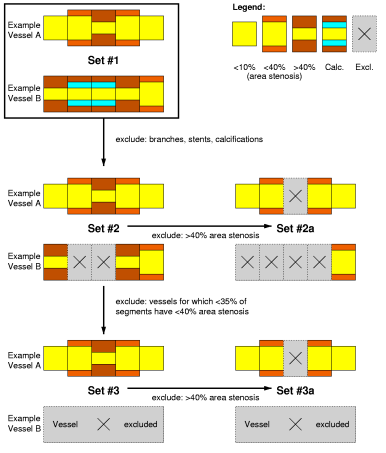
Analysis

- Identification of vessel segments in early stages of atherosclerosis, with *compensatory enlargement:*



outward remodeling >> lumen narrowing >> intervention

- **Hypothesis test:** For the hypothesis to hold, there should be a concentration of vessel locations where relatively *lower* wall shear stress coincides with relatively *higher* plaque accumulation in 10-40% area stenosis range (no lumen narrowing, close to initial WSS values).
- Mark all vessel locations for which area stenosis is within 10-40% range and create the following sets:



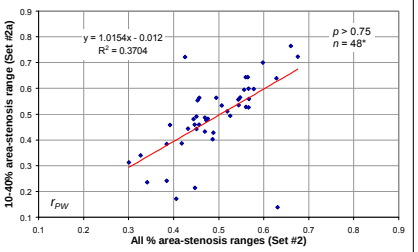
- Set #1 contains all segments of all vessels;
- Set #2 contains all segments of all vessels without branches, stents, or calcifications;
- Set #3 contains all segments for those vessels in Set #2 which have ≥35% of all segments in 10-40% area stenosis range;
- Sets #2a/#3a contain all segments of Sets #2/#3 which are in 10-40% area stenosis range

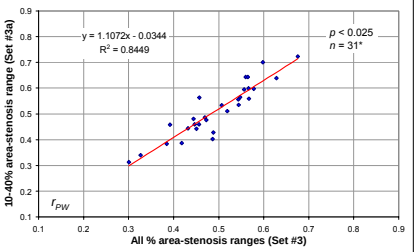
Results

- In each IVUS frame location, 72 circumferential plaque elements are evaluated for:
  - above-average plaque thickness *(a)*
  - below-average plaque thickness *(b)*
  - above-average wall shear stress *(h)*
  - below-average wall shear stress *(l)*
- An *hypothesis validity* index r_{PW} is determined over all segments of a given vessel within a Set.
- r_{PW} quantifies the occurrences *R* where *(a) and (l)* or *(b) and (h)* coincide over all plaque elements :

$$r_{PW} = \frac{\|R_{al} + R_{bh}\|}{\|R_{al} + R_{bh} + R_{ah} + R_{bl}\|}$$

- If the hypothesis holds, r_{PW} is expected to increase for Set #2a over Set #2, and Set #3a over Set #3:



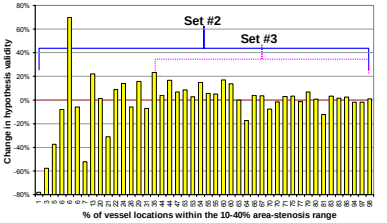


	Increase	no Change (< 1%)	Decrease	Unsuitable*
Sets #2/2a	25	3	16	4
Sets #3/3a	19	3	7	2

*(vessels where either all or no location was in the 10-40% area stenosis range were excluded in the analysis, since *change* is undefined here).

Discussion

- There is no significant change in r_{PW} values between Set #2 and Set #2a covering the full spectrum of disease severity.
- The r_{PW} values significantly increase from Set #3 to Set #3a covering only those vessels which have at least 35% of segments in the 10-40% area stenosis range.
- The 35% threshold was determined empirically from the available data sets by searching for the maximum set providing maximum average increase of r_{PW} (secondary maximum at 22%).
- Best results in the 35-63% range, then increases diminish (Sets #3 and #3a are converging).
- Limited number of subjects.



Conclusions

- It is not possible to see a direct inverse relationship between local wall shear stress and plaque thickness in arteries with a mix of different stages of atherosclerotic disease.
- Automated sorting of vessels and vessel segments by disease severity can isolate those vessel segments which are most likely or unlikely to show the inverse relationship.
- An inverse plaque/wall-shear-stress correlation occurs predominantly in vessel segments that are in early stages of atherosclerosis

Acknowledgements

- Sponsored in part by NIH grant R01 HL63373;
- Rubén Medina, Universidad de Los Andes, Venezuela (plaque morphology analysis);
- Peter Stone, Charles Feldman, Ümit Coşkun, Brigham & Women's Hospital, Northeastern University, Boston (discussions on CFD).

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