An Integrated Morphology+CFD Statistical Investigation of Parent Vessel in Cerebral Aneurysms

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Joint work with M. Piccinelli, T. Passerini (Emory), S. Vantini, L. Sangalli, P. Secchi (Politecnico di Milano, Italy), L. Antiga (Orobix)
Acknowledgments:
ANEURISK
(2005-2008+)

The BA Foundation Project:
Computational and Statistical Analysis of Cerebral Aneurysm Morphology
(2010-2011)
**GOAL:** Analyze the impact of morphology and hemodynamic and morphology on the development (rupture) of the aneurysm

Distinctive features:

a) **Analysis of the parent vessel**

b) **Functional Principal Component Analysis** (see M. Miller plenary) for the investigation of the data & simulations

Deliverable (expected Sept 2011):

A public Brain Aneurysm Images Repository + Data

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STRUCTURE OF THE PROJECT

Clinical Data (DICOM) → GEOMETRICAL ANALYSIS → DATA-BASE

GEOMETRICAL ANALYSIS:
- 3D reconstruction and semi-automatic detection of relevant morphological features

DATA-BASE:
- Clinical Data (DICOM)
- Numerical Modeling
- Statistical Analysis

NUMERICAL MODELING:
- 3D Simulations, FSI, WSS Computation,…

STATISTICAL ANALYSIS:
- Correlation, Functional Data Analysis
Geometrical Reconstruction

Source: Rotational Angiographies from Niguarda Hospital, Italy

Image Manipulation: Vascular Modeling ToolKit (L. Antiga, M. Piccinelli)

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Integrated Morphology+CFD

Statistical Analysis of Parent Vessels in Cerebral Aneurysms
Identification of morphological features

VMTK

Radius

FIGURE 1. A, three-dimensional model of an internal carotid artery (ICA) bearing an aneurysm. B, artery and aneurysmal sac centerlines; a few maximal inscribed spheres are included. C, definition of the ICA bifurcation reference system composed of normal (n), up-normal (u), and origin (o), and the ICA bifurcation plane.
FIGURE 2. A, definition of the aneurysm bifurcation reference system composed of normal ($n_{an}$), up-normal ($u_{an}$), and origin ($o_{an}$) and the aneurysm bifurcation plane. B, in-plane aneurysm bifurcation vectors characterizing the directions of the internal carotid artery and aneurysm branches arriving at and departing from the aneurysm bifurcation. The upstream vector lying on the bifurcation plane is also shown.
FIGURE 3. Local geometrical characterization of the internal carotid artery (ICA). A, representation of the local osculating plane (OP) and the osculating circle tangent to the curve at one point of the ICA centerline. The curvature at each point is defined as the inverse of the radius of the osculating circle. B, rotation of the local osculating plane between 2 points of the siphon centerline.
FIGURE 5. Parameters for the geometric characterization of the internal carotid artery (ICA) and aneurysms with respect to the parent vessel. A, definition of the bend hosting the aneurysm (HB); B, length of the HB; C, radius values along the HB; D, curvature along the HB; E, torsion along the HB; F, position of the aneurysm ostium along the ICA centerline in terms of distance from the ICA bifurcation (absissa) and distance from the HB curvature peak (D_{ost-HB}); G, aneurysm ostium orientation ($\alpha_{ost}$) calculated as the angle between the local ICA oscillating plane normal (OP normal) and the aneurysm bifurcation plane normal ($\nu_{an}$); H, location of the aneurysm on the inner or outer wall of the hosting ICA; I, in-plane angles between the vascular branches arriving at and departing from the aneurysm bifurcation. Computed values are reported for a subset of the parameters.
Bends identification

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# Table 2: Terminology, Symbols, and Descriptions of Geometric Parameters

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HB</td>
<td>The bend hosting the aneurysm</td>
</tr>
<tr>
<td>(l_{HB})</td>
<td>Length of the hosting bend</td>
</tr>
<tr>
<td>(mis_{HB})</td>
<td>Maximum inscribed sphere radius of the hosting bend</td>
</tr>
<tr>
<td>(\alpha_{HB}^{\text{mean}})</td>
<td>Mean curvature of the hosting bend</td>
</tr>
<tr>
<td>(c_{HB}^{\text{mean}})</td>
<td>Maximum curvature of the hosting bend</td>
</tr>
<tr>
<td>(\alpha_{HB}^{\text{max}})</td>
<td>Mean torsion of the hosting bend</td>
</tr>
<tr>
<td>(c_{HB}^{\text{max}})</td>
<td>Torsion value at the proximal hosting bend endpoint</td>
</tr>
<tr>
<td>(\alpha_{HB}^{\text{dist}})</td>
<td>Torsion value at the distal hosting bend endpoint</td>
</tr>
<tr>
<td>(\beta_{HB}^{\text{prox}})</td>
<td>Ratio between inner bend mean torsion value and (c_{HB}^{\text{max}})</td>
</tr>
</tbody>
</table>

**Aneurysm ostium geometric parameters**

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{abs}_{ost})</td>
<td>Curvilinear abscissa of curvature peak of aneurysm host</td>
</tr>
<tr>
<td>(D_{ost-HB})</td>
<td>Distance measured from the plane and the aneurysm host</td>
</tr>
<tr>
<td>(\alpha_{ost})</td>
<td>Angle between 2 planes of the inner wall of the ICA</td>
</tr>
<tr>
<td>(\text{wall}_{ost})</td>
<td>Classification of aneurysm ostium outer wall of the ICA</td>
</tr>
</tbody>
</table>

**Angles between aneurysm bifurcation branches**

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\beta_{upstream})</td>
<td>Angle between the (l_{HB}) and the up-normal unit of the aneurysm vector</td>
</tr>
<tr>
<td>(\beta_{downstream})</td>
<td>Angle between the (l_{HB}) and the downstream branch of the aneurysm vector</td>
</tr>
<tr>
<td>(\beta_{\alpha_{an}})</td>
<td>Angle between the (l_{HB}) and the aneurysm vector</td>
</tr>
</tbody>
</table>

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# Table 3: Mean ± SD, Minimum, and Maximum Values for All Geometric Parameters

<table>
<thead>
<tr>
<th>Geometric Parameter</th>
<th>Mean ± SD</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>(l_{HB})</td>
<td>9.82 ± 5.61</td>
<td>3.10</td>
<td>22.90</td>
</tr>
<tr>
<td>(mis_{HB})</td>
<td>1.90 ± 0.49</td>
<td>0.98</td>
<td>3.83</td>
</tr>
<tr>
<td>(c_{HB}^{\text{mean}})</td>
<td>0.19 ± 0.06</td>
<td>0.08</td>
<td>0.36</td>
</tr>
<tr>
<td>(c_{HB}^{\text{max}})</td>
<td>0.27 ± 0.10</td>
<td>0.11</td>
<td>0.51</td>
</tr>
<tr>
<td>(\alpha_{HB}^{\text{mean}})</td>
<td>0.28 ± 0.10</td>
<td>0.10</td>
<td>0.67</td>
</tr>
<tr>
<td>(\alpha_{HB}^{\text{dist}})</td>
<td>0.68 ± 0.78</td>
<td>0.01</td>
<td>4.40</td>
</tr>
<tr>
<td>(\alpha_{HB}^{\text{prox}})</td>
<td>1.05 ± 0.91</td>
<td>0.23</td>
<td>4.04</td>
</tr>
<tr>
<td>(\beta_{HB}^{\text{BTR}})</td>
<td>0.71 ± 0.19</td>
<td>0.28</td>
<td>1.01</td>
</tr>
<tr>
<td>(\text{abs}_{ost})</td>
<td>-12.73 ± 8.38</td>
<td>-1.70</td>
<td>-39.26</td>
</tr>
<tr>
<td>(D_{ost-HB})</td>
<td>2.08 ± 2.70</td>
<td>0.00</td>
<td>11.30</td>
</tr>
<tr>
<td>(\alpha_{\alpha_{an}})</td>
<td>38.53 ± 22.80</td>
<td>1.51</td>
<td>86.83</td>
</tr>
<tr>
<td>(\beta_{upstream})</td>
<td>10.44 ± 7.44</td>
<td>0.18</td>
<td>31.67</td>
</tr>
<tr>
<td>(\beta_{downstream})</td>
<td>46.59 ± 23.37</td>
<td>4.67</td>
<td>108.78</td>
</tr>
<tr>
<td>(\beta_{\alpha_{an}})</td>
<td>51.35 ± 22.77</td>
<td>4.78</td>
<td>95.19</td>
</tr>
</tbody>
</table>

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*ICA, internal carotid artery.*
Integrated Morphology+CFD

Statistical Analysis of Parent Vessels in Cerebral Aneurysms

Ruptured vs Unruptured

*=statistical significance
Some conclusions

- Ruptured aneurysms of ICA are in a *more distal position*

- Ruptured aneurysms are *close to the peak of curvature* of each segment

- Upstream tracts of the parent vasculature in ruptured aneurysms intersect *aneurysm region with smaller angles*, so that they do align more with the flow divider

- Bends hosting ruptured aneurysms are *shorter, with a smaller radius, a less marked peak of curvature and a less abrupt torsion peak* at the proximal bend boundary compared to those hosting unruptured aneurysms
Fig. 3 Left: first derivatives with respect to the curvilinear abscissa of the centerlines coordinates \((x' = dx/ds, y' = dy/ds, z' = dz/ds)\) of the estimated ICA, reconstructed from images after the free knot interpolation. The black thick curve represents the template reconstructed by the data without alignment. Right: first derivatives of centerlines after the alignment. We identified here just one cluster of data \((k = 1)\). The template of this cluster is represented again by the black thick line.

Fig. 4 Left: boxplots of similarity indexes between each curve and the corresponding template for original estimated centerlines and for centerlines aligned and clustered in \(k\) groups, \(k = 1, 2, 3\). Right: After the alignment, a better clustering is obtained with two groups \((k = 2)\), whose templates are represented by the solid thick lines.
RUPTURED vs UNRUPTURED

L (Lower): Aneurysms *proximal* w.r.t. carotid bifurcation

U (Upper): Aneurysms *distal* w.r.t. carotid bifurcation

R: Ruptured aneurysms
N: Unruptured Aneurysms

<table>
<thead>
<tr>
<th>Group</th>
<th>Size</th>
<th>Position</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ICA</td>
</tr>
<tr>
<td>U</td>
<td>UN</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>UR</td>
<td>16</td>
</tr>
<tr>
<td>L</td>
<td>LN</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>LR</td>
<td>9</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>52</td>
</tr>
</tbody>
</table>

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PCA and Functional PCA

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PCA and Functional PCA

\[ X \in L^2(\Omega; R^n) \quad \Sigma = [\sigma_{ij}] = E[(X_i - \mu_i)(X_j - \mu_j)] = \text{cov}(X_i, X_j) \]

\[ \beta \in R^n \]

\[ \beta_1 = \arg\max_{\beta} \text{var}(\beta'X) \]

\[ \beta_2 = \arg\max_{(\beta : \beta'\Sigma\beta_1=0)} \text{var}(\beta'X) \]

\[ \ldots = \ldots \]

\[ \beta_n = \arg\max_{(\beta : \beta'\Sigma\beta_i=0 \quad \forall i=1,2,\ldots,n-1)} \text{var}(\beta'X) \]

\[ \{\beta_1, \beta_2, \ldots, \beta_n\} = \text{eigenvectors}(\Sigma) \]

\[ X(t) \in L^2(\Omega; L^2([0, T])) \quad \Sigma(t, s) = E[(X(t) - \mu(t))(X(s) - \mu(s))] = \text{cov}(X(t), X(s)) \]

\[ \beta(t) \in L^2([0, T]) \]

\[ \beta_1(t) = \arg\max_{\beta(t)} \text{var}\left(\int_0^T \beta(t)X(t)dt\right) \]

\[ \beta_k(t) = \arg\max_{(\beta(t) : \int_0^T \int_0^T \beta(t)\Sigma(t,s)\beta_i(s)dsdt=0 \quad \forall i=1,2,\ldots,k-1)} \text{var}\left(\int_0^T \beta(t)X(t)dt\right) \]

\[ \{\beta_1(t), \beta_2(t), \ldots\} = \text{eigenfunctions}(\Sigma(t, s)) \]
Some other conclusions (purely morphological analysis)

- ICA hosting proximal aneurysms (L class) are
  - more bended
  - smaller
  - less tapered
  than ICA for U class (distal aneurysms)

- No aneurysms class is similar to L

Analysis reinforcement: Including CFD

Unsteady incompressible Navier-Stokes equations

Hypotheses & Design
Rigid vessel walls: no-slip boundary conditions
Inflow BC: Realistic velocity flow rate
Outflow BC: No-stress conditions

Synthetic description of hemodynamics along the centerline
Average WSS as function of the curvilinear abscissa

\[
\overline{WSS_i}(s_k, t) = \left\| \frac{1}{|\mathcal{S}_k|} \int_{\mathcal{S}_k} WSS_i(x, y, z, t) d\mathcal{S} \right\|
\]
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FPCA Results

Fig. 12 First column: analysis of ICA radius profiles along aligned centerlines. Second column: analysis of curvature profiles of aligned ICA centerlines. Third column: analysis of the first derivative of the WSS profiles along aligned ICA centerlines. First row: aligned profiles. Second row: projections of subject profiles on the corresponding mode of variability. Third row: boxplots of subject scores on these principal components separated per subject group.

Wider ICA

Double bend

Higher WSS peak
SYNTHESIS

**Conjecture**

1) There are two statistical significant clusters of Internal Carotid Arteries, $S$ (2 bends) and $\Omega$ (1 bend)

2) Double Bends probably ``protect” the aneurysms, by dissipating blood energy, resulting in a lower rupture risk
Conclusions:

► GENERAL: Proper **statistical methods** for the integrated
knowledge extraction – numerical simulations treated as
measured data

► SPECIFIC: Some parent vessel features potentially
provide *landmarks for the assessment of a risk of rupture*

**TO DO LIST**

1. Extend the number of variables analyzed (inclusion of the sac – in
   preparation)
2. Extend the number of samples
3. Validate our mechanical interpretation

⇒ **REPOSITORY**