Modeling of Aortic Valve Anatomic Geometry from Clinical Multi Detector-Row Computed Tomography Images
Study Goals

- Measure aortic valve geometry from cardiac CT images
- Compare measurement methods
- Investigate automatic 3D model extraction
  - Use statistical shape models (SSM) and point distribution models (PDM)
Background – Aortic valve

- Aortic valve experiences the highest pressures of the 4 heart valves
- Gateway from left ventricle to the system circuit of the body (Martini 2006)
- Opens approximately 103,000 times per day (Thubrikar 1990)
Aortic Stenosis

- Aortic valve is the most common valve to develop disease
- Aortic stenosis is the most common aortic valve disease
- Stenosis refers to the narrowing of the aortic valve
- Results from atherosclerosis: hardening of the valve leaflets, with eventual calcific nodules developing on the leaflets
  - Valve is slow to open, slow to close. Nodules make it heavier, sclerosis makes it stiffer
  - Valve opening is narrowed
- Effects: aortic stenosis, regurgitation, enlarged aorta, ventricular hypertrophy
Aortic Valve Replacement

- Best long-term treatment is aortic valve replacement
- Traditional method: surgery
  - Surgery effective, but not ideal
    - Need to stop the heart, hookup a heart/lung machine, restart the heart
- New method: transcatheter aortic valve implantation (TAVI)
  - Procedure similar to coronary stent placement. Outpatient. Yay!
  - But the stent is only held in place by friction
Edwards SAPIEN and Medtronic CoreValve
Planning for TAVI

- Surgery: Can directly measure and change replacement valve size during surgery
- TAVI: Must plan in advance. Size differences are big problem
  - Replacement is too small:
    - Paravalvular leakage
    - Stent migration
    - Patient prosthetic mismatch (not enough flow for patient’s size)
  - Replacement is too big:
    - Damage to the aortic annulus
    - Occlusion of the coronary arteries
- Eventual goal to be able to model stent/valve interaction
Volume CT Imaging

- Best method until recently:
  - Transthoracic echocardiography (TTE)
- No radiation

- 64 slice CT can capture all phases of the entire heart in 5-6 heartbeats
- Better than TEE and TTE because it takes more than 1 slice at a time
Clinical assessment (manual 2D measurement)

- Wrote our own 3D measurement program
  - Batching ability... and free!
  - Creates “ground truth” on which other measurement methods can be based

- Step 1 – establish short axis slice plane
2D Manual Measurement Results

Patient Characteristics

Population (n=95)
- Age (years): 57.2 (±12.8)
- Age range: 16 – 85 years
- Gender (M/F): 59 / 36
- Mild stenosis: 7
- % w/diabetes: 15
- % w/hypertension: 33
- % smoker: 10
- % w/high cholesterol: 24
- Calcium score: 146 ±251
- LVEF (%): 64 ±7

Diameters

<table>
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<tr>
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<th>Eccentricity ε</th>
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<td>Annulus minor axis</td>
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<tr>
<td>Sinus</td>
<td>33.5 ±4.7</td>
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<td>at LCA</td>
<td>33.0 ±4.8</td>
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<td>31.9 ±4.6</td>
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<td>Aorta</td>
<td>29.6 ±4.5</td>
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<td>Annulus → LCA</td>
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<td>Annulus → RCA</td>
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<tr>
<td>Annulus → aorta</td>
<td>23.3 ±2.9</td>
</tr>
<tr>
<td>% of patients with</td>
<td></td>
</tr>
<tr>
<td>smaller distance to LCA</td>
<td>74.7% (4.2% equal distances)</td>
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Gender differences

Age differences

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### Comparison to Other Studies

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<tr>
<td><strong>Patient demographics</strong></td>
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<tr>
<td>N</td>
<td>95</td>
<td>26</td>
<td>150</td>
<td>45</td>
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<tr>
<td>% Male</td>
<td>62%</td>
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<td>65%</td>
<td>58%</td>
<td>51%</td>
<td>56%</td>
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<tr>
<td>Age</td>
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<td>54 ±11</td>
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<td>81</td>
<td>61 ±9</td>
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<td><strong>Diameter (mm)</strong></td>
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<tr>
<td>Annulus</td>
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<td>(23.5)</td>
<td>(24.85)</td>
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<td>Annulus (long)</td>
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<tr>
<td>Sinus of Valsalva</td>
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<td>Sino-tubular Junction</td>
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<td>28.1 ±3.1</td>
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<td>25.9 ±3.3</td>
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<td><strong>Height (mm)</strong></td>
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<tr>
<td>Annulus → middle sinus</td>
<td>12.5 ±1.8</td>
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<td>17.2 ±2.7</td>
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<td>-</td>
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<tr>
<td>Annulus → LCA</td>
<td>15.5 ±3.1</td>
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<td>-</td>
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<td>14.9 ±3.2</td>
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<tr>
<td>Annulus → RCA</td>
<td>17.4 ±3.0</td>
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<td>17.2 ±3.3</td>
<td>-</td>
<td>-</td>
<td>16.8 ±3.6</td>
</tr>
</tbody>
</table>

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Hmmmmm... perhaps because they included AS patients? ... But they concluded AS patients were not statistically different from controls.
Alternate measurement methods – 2D automatic

1. Manually draw a line
2. Find intensity profile of that line
3. Find min/max values of that profile
4. Find average $a$ of max/min
5. Threshold image based on $a$
6. Find boundary and centroid of valve
7. Find longest diameter $l$ which passes through centroid
8. Find perpendicular diameter to $l$

<table>
<thead>
<tr>
<th>Diameter (mm)</th>
<th>2D Automatic</th>
<th>2D manual / 2D auto (n=93)</th>
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<tr>
<td></td>
<td>Mean</td>
<td>Eccentricity $\epsilon$</td>
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<tr>
<td>Annulus</td>
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<td>Sinus</td>
<td>32.9 ±4.6</td>
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<td>at LCA</td>
<td>32.6 ±4.6</td>
<td>0.47 ±0.09</td>
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<tr>
<td>at RCA</td>
<td>31.9 ±4.6</td>
<td>0.45 ±0.11</td>
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<tr>
<td>Aorta</td>
<td>29.1 ±4.5</td>
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<table>
<thead>
<tr>
<th>Diameter (mm)</th>
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<th>% error</th>
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<td>Annulus major axis</td>
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<td>5.0%</td>
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<tr>
<td>Annulus minor axis</td>
<td>p=0.010*</td>
<td>4.9%</td>
</tr>
<tr>
<td>Sinus</td>
<td>p=0.337</td>
<td>1.9%</td>
</tr>
<tr>
<td>at LCA</td>
<td>p=0.580</td>
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</tr>
<tr>
<td>at RCA</td>
<td>p=0.952</td>
<td>0.1%</td>
</tr>
<tr>
<td>Aorta</td>
<td>p=0.401</td>
<td>1.9%</td>
</tr>
</tbody>
</table>
Manual 3D measurement

FEM surface generated by mimics segmentation software

Aortic Valve Modeling from MDCT Images

December 15, 2010
### 2D manual measurement comparison

<table>
<thead>
<tr>
<th></th>
<th>2D manual</th>
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<td>Eccentricity ε</td>
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<tr>
<td>Annulus minor axis</td>
<td>20.9 ±2.7</td>
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<td>0.42 ±0.12</td>
<td>32.9 ±4.6</td>
<td>0.44 ±0.09</td>
<td>111.97 ±15.4</td>
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<td>0.47 ±0.09</td>
<td>108.3 ±15.8</td>
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<td>0.45 ±0.11</td>
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<td>95.0 ±14.9</td>
<td>674 ±216</td>
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### 2D manual / 2D automatic (n=93)

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<td>Aorta</td>
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<td>p&lt;0.0001*</td>
<td>3.8%</td>
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### 2D manual / 3D manual (n=75)

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</table>
Novel ways of patient specific modeling

• Simple method: Measure key landmark positions from patient images and interpolate surfaces between using non-uniform rational b-splines (NURBS)
• Now the surface in between landmarks can be matched to an image using boundary detection

• Next step, include the mitral valve.
• Use probabilistic boosting tree, marginal space learning, RANSAC, steerable features, trajectory spectrum learning, PCA, and manifold based motion models

• Ultimate step: Model all four cardiac valves... over the whole cardiac cycle!

• Really useful. Rather complicated. Would take a long time for us to implement a similar method. Besides, we’re only interested in 1 time point for now (70% phase)
Automatic 3D model creation

- How about something simpler?
- Statistical shape models are simple. First introduced in 1995 by Tim Cootes
- Based on the principle that every object of the same type will have a similar shape. The shape varies between the objects, but the statistical variation can be expressed and used in a meaningful way
- For example, hand tracings: Assuming the right hand is traced and no one has injuries or Polydactyly, all objects will have a similar shape.
Statistical shape models

- If landmarks are specified on the models, for example at the tip each finger, statistics about the landmark positions can be calculated.

- Main concept: generate statistics about the shape, deform a mean shape in a manner consistent with the training data.

- The mother of all SSM equations (MOASE):

\[ \mathbf{x} = \bar{\mathbf{x}} + \mathbf{Pb} \]
SSM training procedure

1. Rigidly align all training models (Procrustes)
2. Create mean shape \( \bar{x} = \frac{1}{N} \sum_{i=1}^{N} x_i \)
3. Calculate covariance \( s = \frac{1}{N} \sum_{i=1}^{N} (x_i - \bar{x})(x_i - \bar{x})^T \)
4. Perform PCA to extract Eigenvectors and Eigen values
5. Sum the eigenvalues (\( \lambda \)) to get total variance \( V_T = \sum_{k=1}^{2n} \lambda_k \)
6. Find the largest \( f \% \) of the variance \( \sum_{i=1}^{f} \lambda_i \geq fV_T \)

Now we have:
- Mean shape
- N largest eigenvectors

Let’s create new shapes!
2D SSM example

- Five 2D cross sections of the aortic root

Changing the first mode of variation between +/- 3 S.D. (basically, changing $b$ from the MOASE)
Why create new shapes?

- Remember... the point of SSM is to **deform the mean model in a manner consistent with the training data**
  - That should only give us shapes that are plausible

- **Process for searching using a SSM (simplified)**
  1. Find a new boundary in the target image (using your favorite boundary detection method)
  2. Calculate deformation parameters that will deform the shape to fit the new boundary
  3. Check the fit. Repeat starting at step 1 if necessary until the model has converged

- Now we know how to deform shapes and why. How about 3D?
Downside of SSM in 3D

- Training is significantly more difficult in 3D SSMs
- Traditional 2D training method: hand pick landmark points. Maybe 20 points per image
- 3D method: hand pick landmark points between slices
  - 20 points per slice? By 20 slices?
  - 400 points per 3D volume!

- Picking 400 points is time consuming, but made even harder because features are on different slices... lots of flipping through slices
- Either need a really simple model, or a way to do landmarking once and propagate those landmarks to all training data
How to do landmark propagation?

1) create a template model from a template image
2) warp all training images to the template image
   2.1) record the deformation field
3) apply the inverted warp for each image to the template model
4) now all training images have been landmarked

A similar method was used by van Assen (2006) to do automatic landmarking

Images were registered to a template image (translate, rotate, scale). Then the inverse registration applied to propagate the template coordinates to all training datasets.
Landmark Propagation

Training (B) → Template (A)

Image B → warp → Image A

Generate Jacobian determinant (lookup table)

Coordinates B → Lookup table → Coordinates A
Developed by John Ashburner in 1999 to perform 3D warping of brain MRIs to a common brain atlas... so that brain activation from fMRI studies can be mapped to known brain regions.
This tool was used as a black box, with only two input parameters:
- Warping regularization, which controls how much warping is allowed
- Number of iterations, which is the number of times it runs the warping algorithm

Brief under-the-hood concepts:
- Principle of HDW is that the deformation field from image A to B must be the inverse of B to A
- A maximum a posteriori (MAP) approach is used, which utilizes a Bayesian framework
  \[
  p(Y|b) \propto p(b|Y)p(Y)
  \]
  where \( b \) is the data and \( Y \) are the parameters to deform the image
  - \( p(Y) \) is the probability of parameters \( Y \)
  - \( p(b|Y) \) is the probability of data \( b \) given parameters \( Y \)
  - \( p(Y|b) \) is the probability of given parameters \( Y \) data \( b \)
- maximum a posteriori estimate is the value of \( Y \) that maximizes \( p(Y|b) \)
High dimensional warping for landmark propagation

1. Manually pick center of sinus for all images
2. Crop all images to a sphere 80mm diameter centered in the sinus
3. Realign all images to template
4. Warp all images to the template image
5. Build a model of the template (1446 points)
6. Inverse warp of the template coordinates $\rightarrow$ landmark propagation
7. Create mesh models for all images
HDW in practice

- Neat process, but we only have access to two parameters to control deformation: regularization $\lambda$ and number of iterations.
- Lower $\lambda$ allows more movement when warping, so we went with 0.5 instead the default of 4 for brains, but we stuck with the default 8 iterations.
- **HDW treated as a black box**
- In the end it nicely writes out Jacobian transformation images, which can be used as a lookup table
Landmark propagation

- Jacobian images are actually three 3D volumes
  - Volume 1 – x coordinate lookup
  - Volume 2 – y coordinate lookup
  - Volume 3 – z coordinate lookup

- Want to find where point p was before warping? (inverse warp)
  - From volume 1, find the intensity of point p... that is now the x coordinate before it was warped to the template
  - Do the same for volumes 2,3 and get coordinates y and z

Sample view of volume 1

Intensity of red cross is 38.11, but x plane of image is 40, so the coordinate at that point was shifted 1.89mm in the x direction during deformation

\[ x_{new} = \text{Jacobian}(x_{old}, y_{old}, z_{old}, 1) \]
Point distribution models

- Now, *in theory*, we have 95 properly landmarked training sets. *We’ll examine how effective HDW was later...*

- Remember the active shape model thingy with the arrows? How about in 3D, with valves!

- How about some statistics of shape?? Now that’s easy to do

**Algorithm to create Point distribution models**

1. Align all models to the first model. Then place in one giant array
   \[ S = (x_{11}, \ldots, x_{n1}, y_{11}, \ldots, y_{n1}, z_{11}, \ldots, z_{n1}; \quad x_{12}, \ldots, x_{n2}, y_{12}, \ldots, y_{n2}, z_{12}, \ldots, z_{n2}, \ldots) \]
2. Calculate covariance \( C \) of \( S \)
3. Calculate PCA on \( C \), generate eigenvectors & eigenvalues
4. Determine the eigenvectors that describe the top 98% of the variance
**HDW effectiveness**

- Visual inspection seemed to show HDW worked well, however it was found that it did not perform well with large warps.

- Did not successfully warp images where structures were more than 2-3mm apart

- How about comparing warping effectiveness among similar sized valves?

<table>
<thead>
<tr>
<th></th>
<th>Annulus warped mean</th>
<th>manual mean</th>
<th>Paired t-test</th>
<th>% difference</th>
<th>Sinus warped mean</th>
<th>manual mean</th>
<th>Paired t-test</th>
<th>% difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (N=95)</td>
<td>28.2 ±0.6</td>
<td>24.4 ±2.7</td>
<td>P&lt;0.0001</td>
<td>16%</td>
<td>33.3 ±1.4</td>
<td>33.6 ±4.6</td>
<td>P=0.4598*</td>
<td>0.8%</td>
</tr>
<tr>
<td>Annulus matched (24.2 - 28.2 mm, N=42)</td>
<td>28.4 ±0.6</td>
<td>25.8 ±1.1</td>
<td>P&lt;0.0001</td>
<td>10%</td>
<td>33.9 ±1.2</td>
<td>35.6 ±3.5</td>
<td>P=0.0018</td>
<td>4.7%</td>
</tr>
<tr>
<td>Sinus matched (29.2 - 33.2 mm, N=29)</td>
<td>28.0 ±0.4</td>
<td>23.3 ±1.7</td>
<td>P&lt;0.0001</td>
<td>20%</td>
<td>32.9 ±0.8</td>
<td>31.3 ±0.9</td>
<td>P&lt;0.0001</td>
<td>5.1%</td>
</tr>
<tr>
<td>Annulus &amp; sinus matched (N=9)</td>
<td>27.9 ±0.4</td>
<td>25.2 ±1.0</td>
<td>P&lt;0.0001</td>
<td>11%</td>
<td>32.9 ±0.9</td>
<td>31.7 ±0.7</td>
<td>P=0.0317</td>
<td>3.8%</td>
</tr>
</tbody>
</table>

* indicates results are not significantly different
Warping effectiveness

- **template**
- **good fit** (<1 mm offset)
- **moderate fit** (1-2 mm offset)
- **bad fit** (>4 mm offset)
Using the mother of all SSM equations... we can create new shapes

Standard deviation from the mean can be calculated from the square root of the Eigen values

By varying \( b \) within \( x \) standard deviations from the mean, the shape can be varied

Shown in next 2 slides

The inverse can also be done: If a new shape is known, the \( b \) can be calculated

Useful during searching

\[
x = \overline{x} + Pb
\]
PDM creation – all models

All PDMs took approximately 9 minutes to generate on an Intel Dual Core 3.16GHz CPU

- **Green** – mean model
- **Red** – model altered by changing the first mode of variation by + 5 standard deviations from the mean
- **Blue** – model altered by changing the first mode of variation by - 5 standard deviations from the mean

All models (n=95)

- 64 modes of variation

All scaled models (n=95)

- 1 mode of variation
PDMs – from valves with similar sizes

Annulus matched (n=42)  
33 modes of variation

Sinus matched (n=29)  
24 modes of variation

Annulus & sinus matched (n=9)  
8 modes of variation
Conclusion

- 2 steps closer to modeling a patient specific valve-stent interaction
  - Measured real 3D images from patient population
  - Identified effective methods for measurement
  - Began 3D model extraction process

- HDW appears to work well enough to eliminate the need to manually landmark 3D training data
  - Save time!
Future Work

- Improve warping accuracy by using DARTEL toolbox to perform warping on segmented data
- Apply the training data to search real target images
- Implement 3D AAM/ASM
- Maybe try some of the neat methods by Ionasec et al
- Scale images before warping, then unscale when unwarping

- Eventual goal: expand a virtual stent inside a patient-specific valve model
Acknowledgements

- Qian Wang
- Sonia Ortiz
- Charles Primiano MD
- Wei Sun PhD
- Hartford Hospital PACS team
- Hartford Hospital Cardiac Catheterization Lab
- Wendy Book MD
References

Questions?
Extra slides after this... if needed
Prior potentials are calculated assuming the image pixels are nodes in a grid with a triangular mesh.

A 3x3 affine mapping $\mathbf{M}$ between images $x$ and $y$:

$$
\mathbf{M} = \begin{bmatrix}
m_{11} & m_{12} & m_{13} \\
m_{21} & m_{22} & m_{23} \\
0 & 0 & 1
\end{bmatrix} = \begin{bmatrix}
y_{i1} & y_{i2} & y_{i3} \\
y_{21} & y_{22} & y_{23} \\
x_{11} & x_{12} & x_{13} \\
x_{21} & x_{22} & x_{23}
\end{bmatrix}^{-1}
$$

then a Jacobian matrix $\mathbf{J}$ can be obtained from $\mathbf{J} = \begin{bmatrix} m_{11} & m_{12} \\ m_{21} & m_{22} \end{bmatrix}$

and a penalty for each triangle, where $s$ is the triangle area and $\lambda$ is a regularization parameter

$$
h = \lambda (1 + |\mathbf{J}|) (\log(s_{11})^2 + \log(s_{22})^2) / 2
$$

prior potential of the whole image is the sum of the penalties

$$
H(Y) = \sum_{i=1}^{f} h_i
$$

Finally, the deformation parameters $Y$ are iteratively estimated by

$$
y_i^{(n+1)} = y_i^{(n)} - \varepsilon \frac{\partial H(Y | \mathbf{b})}{\partial y_i} = y_i^{(n)} - \varepsilon \left( \frac{\partial H(\mathbf{b} | Y)}{\partial y_i} + \frac{\partial H(Y)}{\partial y_i} \right)
$$

where $n$ is the iteration number, $i$ is the element number of $Y$, and $\varepsilon$ is a small number. Basically this iterative process which moves nodes in a direction that minimizes the a posteriori potential.