Added value of a statistical atlas-based quantification of motion abnormalities for the prediction of CRT response

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(4) ICREA, Spain
Why quantifying abnormalities? CRT context

- Lack of reproducibility in large scale studies [1]
- Is there a “universal” index? [2,3,4]
- Changing the strategy?

[5] Non-responders with the current guidelines:
- 30% (clinical response)
- 50% (echo response)

- Ejection fraction <35%
- QRS duration >120ms
- NYHA classification (II)-III-IV

[1] Stellbrink et al., EHJ Suppl. 2004
[2] Chung et al., Circulation 2008
Why quantifying abnormalities? CRT context

- Lack of reproducibility in large scale studies [1]
- Is there a “universal” index? [2,3,4]
- Changing the strategy?

Patient classification into specific etiologies of HF [6]

- Correction of specific mechanisms of dyssynchrony conditions response
- Predictive value of specific classes
  - Septal flash [6,7]
  - Septal rebound stretch [8]
  - Apical transverse motion [9]

[1] Stellbrink et al., EHJ Suppl. 2004
[2] Chung et al., Circulation 2008
[6] Parsai et al., EHJ 2009
[7] Parsai et al., EHJ 2009
[9] Voigt et al., EHJ 2009

[5] Non-responders with the current guidelines:
  - 30% (clinical response)
  - 50% (echo response)
What is a “septal flash”?

Fig. 3: Septal flash mechanism

Healthy volunteer

CRT candidate with SF

Healthy volunteer

CRT candidate with SF

OFF
Effect of CRT on septal flash

Pre-CRT

Follow-up (6 months)
Why quantifying abnormalities? CRT context

- Lack of reproducibility in large scale studies [1]
- Is there a “universal” index? [2,3,4]
- Changing the strategy?

- Correction of specific mechanisms of dyssynchrony conditions response
- Predictive value of specific classes

The ability of accurately identifying a SF will fully condition its predictive value

How to identify a SF? [6,7]
Is visual inspection enough?

[1] Stellbrink et al., EHJ Suppl. 2004
[2] Chung et al., Circulation 2008
[6] Parsai et al., EHJ 2009
[7] Parsai et al., EHJ 2009
[9] Voigt et al., EHJ 2009
How to identify a SF? Is visual inspection enough?

- Mid inferoseptal
- Apical septal
- Basal inferoseptal

???
How to identify a SF? Is visual inspection enough?

Large – whole septum

Small – whole septum

Large – basal septum

Ambiguous
Statistical atlases: new concept for cardiac studies

ATLAS = average + statistical representation of variability within a population

[10] Ordas et al., ISPA 2006
[12] De Craene et al., FIMH 2009
Atlas-based quantification of motion abnormalities

Healthy subjects

Atlas

Radial velocity

Long. velocity

average

variance

ECG

[14] Duchateau et al., ESC 2010
Atlas-based quantification of motion abnormalities

Atlas

Healthy subjects

Patient to study

Radial velocity

Long. velocity

ECG

p-value (log scale)

[14] Duchateau et al., ESC 2010
Data representation

Local maps at fixed time $t$

- End diastole (1)
- Septal activation (2)
- Lateral activation (3)
- Ejection (4)

- Inward
- Outward

Temporal evolution at a fixed anatomical point

- $p$-value (log scale)

Red = large abnormality
Data representation

Spatiotemporal maps of abnormality

Blue = Inward (vp<0)
Red = Outward (vp>0)

[15] Duchateau et al., STACOM-MICCAI 2010
Contributions

- **New** quantitative indexes [quantification of motion abnormalities]

**Statistical atlas: added-value for clinical studies**
- Automatic, **reproducible**
- Information still available at every location \((x,t)\) [not heart segments only]
- Intrinsic **comparison to “normality”**

- **Generic** methods applicable to almost any
  - imaging modality
  - studied parameter and mechanism

**In this work:**  **Quantification** of a specific pattern: **septal flash (SF)**
Patient population

21 Healthy volunteers

≈ 60 frames/s
0.24 x 0.24 mm²

2D echo, 4-chamber view

88 candidates OFF / ON / FU (11 ± 2 months)
EF < 35%, QRS duration > 120ms, and (or) NYHA class III-IV

≈ 30 frames/s
0.24 x 0.24 mm²

CRT response:

Clinical

6min walking test increase ≥ 10%
or NYHA class reduction ≥ 1 point

Echocardiographic

LV end-systolic volume reduction ≥ 15%

(in alive patients without heart transplantation)
### Patient population

<table>
<thead>
<tr>
<th>CRT candidates</th>
<th>Volunteers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
</tr>
<tr>
<td>Number</td>
<td>88</td>
</tr>
<tr>
<td>Age (years)</td>
<td>68 ± 9</td>
</tr>
<tr>
<td>Male gender</td>
<td>64 (73 %)</td>
</tr>
<tr>
<td>QRS width (ms)</td>
<td>178 ± 29</td>
</tr>
<tr>
<td>6min walking test (m)</td>
<td>289 ± 82</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>0</td>
</tr>
<tr>
<td>II</td>
<td>23 (26 %)</td>
</tr>
<tr>
<td>III</td>
<td>59 (64 %)</td>
</tr>
<tr>
<td>IV</td>
<td>7 (8 %)</td>
</tr>
<tr>
<td>LV end-diastolic volume (mL)</td>
<td>247 ± 88</td>
</tr>
<tr>
<td>LV end-systolic volume (mL)</td>
<td>186 ± 76</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>25 ± 8</td>
</tr>
</tbody>
</table>

**CRT response:**

**(in alive patients without heart transplantation)**

**Clinical**  
6min walking test increase ≥ 10%  
or NYHA class reduction ≥ 1 point

**Echocardiographic**  
LV end-systolic volume reduction ≥ 15%
New quantitative indexes [quantification of motion abnormalities]

Statistical atlas: added-value for clinical studies
- Automatic, reproducible
- Information still available at every location \((x,t)\) [not heart segments only]
- Intrinsic comparison to “normality”

Some questions to answer

a) PV-maps vs visual inspection: agreement?

b) Predicitive value of SF at baseline? Visually Atlas-based

c) Evolution after the therapy?
PV-maps vs visual inspection: agreement?

Maps-based

<table>
<thead>
<tr>
<th></th>
<th>SF</th>
<th>No SF</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF</td>
<td>57</td>
<td>1</td>
</tr>
<tr>
<td>No SF</td>
<td>4</td>
<td>26</td>
</tr>
</tbody>
</table>

Cohen’s Kappa = 0.87
Observed agreement = 0.94
**Predicitive value of SF at baseline?**

<table>
<thead>
<tr>
<th></th>
<th>Responders</th>
<th>Clinical response</th>
<th>Echocardiographic response</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Clinical</td>
<td>Echo</td>
</tr>
<tr>
<td>CRT</td>
<td>88</td>
<td>72</td>
<td>52</td>
</tr>
<tr>
<td>SF (M-mode)</td>
<td>58</td>
<td>50</td>
<td>44</td>
</tr>
</tbody>
</table>

* Positive predictive value = percentage of responders among the considered subset of patients

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**Response rate with the current guidelines:**

- 0.7 (clinical response)
- 0.5 (echo response)

- Ejection fraction <35%
- QRS duration >120ms
- and/or NYHA classification III-IV

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Predictive value of SF at baseline?

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<th>Clinical response</th>
<th>Echocardiographic response</th>
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<td>58</td>
<td>50</td>
</tr>
<tr>
<td>SF (atlas)</td>
<td>60</td>
<td>52</td>
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**Improved prediction using atlas tools?**

**[8] Response rate with the current guidelines:**
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- 0.5 (echo response)

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## Predictive value of SF at baseline?

<table>
<thead>
<tr>
<th>Study</th>
<th>CRT #</th>
<th>SF #</th>
<th>Response rate</th>
<th>LVESV reduction ≥ 15%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duchateau, EuroEcho 2010</td>
<td>88</td>
<td>58</td>
<td>0.76 (visual)</td>
<td>LVESV reduction ≥ 15%</td>
</tr>
<tr>
<td></td>
<td>88</td>
<td>60</td>
<td>0.75 (atlas)</td>
<td>LVESV reduction ≥ 15%</td>
</tr>
<tr>
<td>Cikes, HSF 2009</td>
<td>5</td>
<td>5</td>
<td>1</td>
<td>LVESV reduction ≥ 10%</td>
</tr>
<tr>
<td>Cikes, ESC 2010</td>
<td>12</td>
<td>12</td>
<td>1 ?</td>
<td>LVESV reduction ≥ 10%</td>
</tr>
<tr>
<td>Doltra, ESC 2010</td>
<td>80</td>
<td>35</td>
<td>0.8</td>
<td>LVESV reduction ≥ 15%</td>
</tr>
<tr>
<td>Parsai, EHJ 2009</td>
<td>161</td>
<td>87</td>
<td>0.89</td>
<td>NYHA Class reduction ≥ 1 OR LVESV reduction ≥ 10%</td>
</tr>
<tr>
<td>Parsai, EHJ 2009</td>
<td>52</td>
<td>36</td>
<td>1</td>
<td>LVESV reduction ≥ 10%</td>
</tr>
<tr>
<td>Abdul-Jawal, SEC 2010</td>
<td>34</td>
<td>23</td>
<td>0.61</td>
<td>EF increase ≥ 6% OR ED diameter reduction ≥ 15%</td>
</tr>
</tbody>
</table>

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**Response rate with the current guidelines:**

- **0.7** (clinical response)
- **0.5** (echo response)

---

- Ejection fraction <35%
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Evolution after the therapy

CRT #9
Septal flash

CRT #8
Septal flash

CRT #12
Left-right interaction

OFF

Local p-value (log scale)

Follow-up

Blue = Inward (vp<0)
Red = Outward (vp>0)
Evolution after the therapy

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Septal flash

CRT #8
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Left-right interaction

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Follow-up

Local p-value (log scale)

Blue = Inward (vp<0)
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- Correction of specific mechanisms of dyssynchrony conditions response \[9,10\]

[6] Parsai et al., EHJ 2009
[7] Parsai et al., EHJ 2009

Blue = Inward (vp<0)
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Conclusions

a) PV-maps vs visual inspection: agreement?

b) Predictive value of SF at baseline?  

Visually  
Atlas-based

c) Evolution after the therapy?

- New quantitative indexes [quantification of motion abnormalities]

- Statistical atlas: added-value for clinical studies
  - Automatic, reproducible
  - Information still available at every location \((x,t)\) [not heart segments only]
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Acknowledgements

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Thanks !...Any questions?