Cardiología Nuclear: su aplicación en el estudio de la sincronía ventricular

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*receives royalties from the sale of the following software programs: Emory Cardiac Toolbox, PERFEX, Heartfusion, Synctool and ExSPECT II.
* Consultant for Lantheus
*receives research funding from GE, and has an equity position with Syntermed inc.
SPECT usado en Disincronía sistólica intraventricular

• Como medirlo con IPM
• Que exactitud tiene
• Cuales son las características clínicas
• Como usarlo para predecir la respuesta al TRC y para guiar donde colocar el electrodo del TRC
Sincronismo de la contracción ventricular: El Instante de la Contracción Homogénea

- Instante cuando la onda eléctrica de activación llega al segmento que se contrae (onda eléctrica)
- Instante cuando el segmento que se contrae se empieza a engrosar (onda mecánica)
- Instante cuando la pared miocárdica correspondiente se empieza a mover (onda mecánica)
MUGA: Analisis de Fase
Categorías de Disincronías Cardíacas

• Atrio-ventricular
  – AV dyssynchrony, the result of conduction delay in the AV node, results in a delay between atrial and ventricular contraction, mitral regurgitation in late diastole, shortened ventricular filling time and concomitant occurrence of atrial systole with early passive filling and hence reduced LV filling time.

• Inter-ventricular
  – Inter-ventricular dyssynchrony results in right ventricular (RV) activation preceding LV contraction; the earlier RV contraction results in displacement of the septum toward the LV cavity, abnormal septal motion, abnormal septal perfusion and decreased cardiac efficiency.

• Intra-ventricular
  – Intra-ventricular dyssynchrony is manifested by portions of the LV myocardium being activated early while other portions late during the cardiac cycle. The early contraction occurs when pressure is low and does not lead to ejection while late contraction occurs at higher stress and results in passive stretch of the early contracting segments. These alterations again result in decline in LV efficiency
Con que exactitud podemos medir el engrosamiento?

- Using partial volume effect: $\Delta \text{cts} \sim \Delta \text{thickness}$


Nichols et al:

**Conclusion.** No convincing evidence was found of thickness above the partial volume limit in this large sample of 75 normotensive and 25 hypertensive patients. Therefore it is likely that relations between myocardial count increases and wall thickening are similar throughout the cardiac cycle, even in patients with left ventricular hypertrophy. (J Nucl Cardiol 1998;5:484-90)
Gated-SPECT de Perfusion Miocardica: Analisis del Engrosamiento de la Pared durante la Sistole

Temporal Sampling

Counts

Phase

Thickening

Data from cardiac cycle
1st harmonic of FFT
DC component of FFT


Ejemplo Normal
Table 1. Normal limits of OMC phases

<table>
<thead>
<tr>
<th></th>
<th>Cutoff</th>
<th>Range</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak phase (°)</td>
<td>43°</td>
<td>6.3-27.6</td>
<td>14.2</td>
<td>5.1</td>
</tr>
<tr>
<td></td>
<td>135°</td>
<td>5.1-31.4</td>
<td>11.8</td>
<td>5.2</td>
</tr>
<tr>
<td>Phase SD (°)</td>
<td></td>
<td>Ancho de Banda</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>43°</td>
<td>22-81</td>
<td>38.7</td>
<td>11.8</td>
</tr>
<tr>
<td></td>
<td>135°</td>
<td>18-62</td>
<td>30.6</td>
<td>9.6</td>
</tr>
<tr>
<td>Histogram skewness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.84-5.95</td>
<td>4.19</td>
<td>0.68</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.05-6.10</td>
<td>4.60</td>
<td>0.72</td>
<td></td>
</tr>
<tr>
<td>Histogram kurtosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8.45-45.32</td>
<td>19.72</td>
<td>7.68</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9.65-48.19</td>
<td>23.21</td>
<td>8.16</td>
<td></td>
</tr>
</tbody>
</table>

Chen et al, JNC 2005;12:687-95
Henneman MM, Chen J, et al. JNM 2007; 48:1104-1111
Parámetros de fase

Parámetros cuantitativos del HF:
(Evaluación de la fase con Synctool)

- Pico de fase (PF),
- Desviación estandar (SD)
- Amplitud del histograma (HB),
- Simetría de la distribución (HS)
- Kurtosis (HK).

ANÁLISIS DE FASE DE LA GATED-SPECT DE PERFUSIÓN MIOCÁRDICA EN DIVERSAS PATOLOGÍAS CARDÍACAS AISLADAS. MN. Pizzi, Hospital Universitari Vall d`Hebron, Barcelona.

Vall d'Hebron
Hospital General
Cardiología Nuclear
Análisis de la Fase del Gated-SPECT de Perfusión Miocárdica

- Phase analysis of ECG-gated myocardial perfusion imaging (MPI) had been developed to measure left-ventricular dyssynchrony
- Preliminary normal limits had been generated

Chen et al, J Nucl Cardiol 2005;12:687-95
Ejemplo: Bloqueo de RI (LBBB)
Automatic Global and Regional Phase Analysis from Gated Myocardial Perfusion SPECT Imaging: Application to the Characterization of Ventricular Contraction in Patients with Left Bundle Branch Block

Serge D. Van Kriekinge, Hidetaka Nishina, Muneo Ohba, Daniel S. Berman, and Guido Germano

*Department of Imaging and Medicine, Cedars-Sinai Medical Center, Los Angeles, California; †Division of Cardiology, Tokyo Medical University, Japan; and ‡Heart Center, Tatsuno Kofukai Medical Research Institute, Tokyo, Japan

Although many patients with heart failure benefit from cardiac resynchronization therapy (CRT), predicting which patients will respond to CRT remains challenging. Recent evidence suggests that the analysis of mechanical dyssynchrony using gated myocardial perfusion SPECT (MPS) may be an effective tool. The aim of this study was to examine global and regional gated MPS dyssynchrony measurements by comparing parameters obtained from patients with low likelihood of conduction abnormalities. Ejection fraction (EF) and coronary artery disease and patients with left bundle branch block (LBBB). Methods: A total of 86 consecutive patients with LBBB and 72 consecutive patients with LBBB, all without prior myocardial infarction or sternotomy, were studied using gated MPS. Global (histogram SD [r]), bandwidth [b], and entropy [e] and regional (wall- and segment-based differences of means of M$_{AW}$ and M$_{SB}$, respectively) or modes of M$_{MG}$ and M$_{MS}$, respectively) dyssynchrony measures were calculated by Fourier harmonic analysis of local myocardial contractility.

Alternative methods for the assessment of mechanical dyssynchrony using phase analysis of gated single photon emission computed tomography myocardial perfusion imaging

Wael AlMarzouki, Wael A. Jaber, Richard A. Grimm, Thomas Marwick, and Manuel D. Cerqueira

Received: 12 August 2011 / Accepted: 7 October 2011

Abstract Measurement of left ventricular (LV) mechanical dyssynchrony from single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) allows optimization of cardiac resynchronization therapy in heart failure patients. We compared the discriminatory ability and reproducibility of a new software method, Corridor 4DM (4DM) to the established method, Emory Cardiac Toolbox (ECTB) in normals and heart failure patients. LV dyssynchrony was measured in 100 control (Group 1) and 100 patients with LVEF <35% (Group 2) using time to peak thickening with first harmonic, fourth harmonic, and volume curve methods with the 4DM software, and compared to ECTB. Of the 3 4DM methods, first harmonic had the best correlation with the ECTB (R = 0.88, slope = 1.00, P < 0.0001, bias = 0.18 [95% CI = -20°; 16°] for phase standard deviation), and similarly for histogram bandwidth, while volume curve analysis had the greatest variation. The intra and inter-observer reproducibility for 4DM time to peak thickening with first harmonic was very good (R = 0.99, P < 0.0001) and coefficient of variability 10% [95% CI, 9.2–11.8%] for intra-observer, and R = 0.97, P < 0.0001, coefficient of variability 16% [15–17%] for inter-observer, respectively. Finally, in patients with LVEF <35%, the area under the curve on receiver operator characteristic analysis was 0.93 [95% CI: 0.89–0.97] to detect significant mechanical dyssynchrony (i.e. standard deviation ≥83%) using 4DM versus ECTB. The 4DM-software provides an accurate and reproducible alternative method of dyssynchrony analysis of SPECT MPI for evaluation and management of heart failure.

Keywords Phase analysis · Dyssynchrony · Corridor 4DM · Single photon emission computed tomography
ANÁLISIS DE FASE DE LA GATED-SPECT DE PERFUSIÓN MIOCÁRDICA EN DIVERSAS PATOLOGÍAS CARDÍACAS AISLADAS.

MN. Pizzi, Hospital Universitari Vall d’Hebron, Barcelona.

Ejemplos clínicos

2-Hemibloqueos (HBR): 20

3-Bloqueo de rama derecha (BRD): 40

4-Bloqueo de rama izquierda (BRI): 37

5-Marcapasos (MCP): 26

6-Infarto del miocardio (IM): 71

7-Miocardiopatía dilatada (MD): 17
Podemos medir con exactitud cambios temporales usando 8 cuadros por ciclo cardiaco?

- Using sampling theorem: replaces a discrete periodic function with a continuous one
  - Frames needed: $1^{st}$ Harmonic (sine) = 3, $2^{nd}$ Har = 5, $3^{rd}$ Har = 7

- Chen et al, J Nucl Cardiol 2008; 15: 383-391
  - 8 frames has equivalent temporal resolution of $1/64^{th}$ of the cardiac cycle
Análisis de Fourier del Engrosamiento Sistólico usando el 1er armónico

Cuentas por cuadros más importante que cuadros por ciclos cardiacos
Podemos medir con exactitud cambios de fase en regiones con pocas cuentas?

Table 2. Paired t-test for regions of 10% uptake perfusion activity

<table>
<thead>
<tr>
<th>LV phase shift</th>
<th>60</th>
<th>40</th>
<th>20</th>
<th>−20</th>
<th>−40</th>
<th>−60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal uptake</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean phase ± SD</td>
<td>55.7 ± 15.1</td>
<td>31.5 ± 15.7</td>
<td>23.7 ± 12.6</td>
<td>−20.7 ± 11.3</td>
<td>−37.9 ± 19.8</td>
<td>−59.4 ± 16.1</td>
</tr>
<tr>
<td>Average SNR</td>
<td>35.82</td>
<td>28.13</td>
<td>29.98</td>
<td>27.54</td>
<td>32.91</td>
<td>35.20</td>
</tr>
<tr>
<td>10% uptake</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean phase ± SD</td>
<td>57.6 ± 13.7</td>
<td>34.1 ± 16.7</td>
<td>24.7 ± 12.4</td>
<td>−24.5 ± 13.3</td>
<td>−34.3 ± 16.4</td>
<td>−56.9 ± 16.5</td>
</tr>
<tr>
<td>Average SNR</td>
<td>12.61</td>
<td>12.54</td>
<td>12.87</td>
<td>12.97</td>
<td>13.75</td>
<td>12.92</td>
</tr>
<tr>
<td>P</td>
<td>.17</td>
<td>.21</td>
<td>.18</td>
<td>.21</td>
<td>.15</td>
<td>.11</td>
</tr>
</tbody>
</table>

Cheung et al
The performance of phase analysis
J Nucl Cardiol 2012; 19: 500-506
Podemos medir con exactitud cambios de la fase en regiones con pocas cuentas?


Aljaroudi et al, J Nucl Cardiol 2011; 18: 36-42
LV dyssynchrony measured by phase analysis was compared to that measured by Tissue Doppler Imaging (TDI) in 75 heart failure patients.

Phase standard deviation and histogram bandwidth correlated well with TDI LV dyssynchrony.

Podemos reproducir los parámetros de la fase entre 2 reconstrucciones?

In 50 normal and 50 LV dysfunction patients recons twice

<table>
<thead>
<tr>
<th></th>
<th>Normal controls</th>
<th>LV dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Manual base</td>
<td>Manual base</td>
</tr>
<tr>
<td></td>
<td>( N=50 )</td>
<td>( N=50 )</td>
</tr>
<tr>
<td><strong>Phase SD (°)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD of the first reading</td>
<td>8.6 ± 2.9</td>
<td>41.6 ± 24.2</td>
</tr>
<tr>
<td>Absolute difference (mean ± SD) of the two readings</td>
<td>1.2 ± 1.2</td>
<td>6.0 ± 7.3</td>
</tr>
<tr>
<td>Intraclass correlation coefficient of the two readings</td>
<td>0.85</td>
<td>0.93</td>
</tr>
<tr>
<td><strong>Bandwidth (°)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD of the first reading</td>
<td>27.9 ± 8.9</td>
<td>115.4 ± 60.5</td>
</tr>
<tr>
<td>Absolute difference (mean ± SD) of the two readings</td>
<td>3.6 ± 3.7</td>
<td>26.5 ± 40.2</td>
</tr>
<tr>
<td>Intraclass correlation coefficient of the two readings</td>
<td>0.84</td>
<td>0.73</td>
</tr>
</tbody>
</table>
Podemos reproducir los parámetros de la fase entre 2 adquisiciones?

In 30 patients imaged twice 30 min apart – all parameters $r > .9$
Lin et al, J Nucl Cardiol 2010, 17: 811-6

<table>
<thead>
<tr>
<th>N = 30</th>
<th>PSD</th>
<th>PHB</th>
<th>LVEF</th>
<th>LVESV</th>
<th>LVEDV</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\mu$</td>
<td>.58°</td>
<td>2.03°</td>
<td>-.37%</td>
<td>2.20 mL</td>
<td>2.73 mL</td>
</tr>
<tr>
<td>$\sigma$</td>
<td>5.11°</td>
<td>13.77°</td>
<td>3.92%</td>
<td>8.42 mL</td>
<td>10.94 mL</td>
</tr>
<tr>
<td>$P$</td>
<td>.541</td>
<td>.425</td>
<td>.612</td>
<td>.163</td>
<td>.182</td>
</tr>
<tr>
<td>$r$</td>
<td>.979</td>
<td>.976</td>
<td>.982</td>
<td>.996</td>
<td>.994</td>
</tr>
<tr>
<td>CV</td>
<td>8.8%</td>
<td>8.7%</td>
<td>9.2%</td>
<td>8.7%</td>
<td>5.4%</td>
</tr>
</tbody>
</table>

PSD = phase std dev, PHB = phase histogram bandwidth, $\mu$ = mean difference, $\sigma$ = std dev of difference, $P < .05$ stat significance, $r$ = correlation coefficient, CV = average coefficient of variability
Podemos medir con exactitud cambios de la fase en tejido isquémico?

Aljaroudi et al, J Nucl Cardiol 2011; 18: 36-42
Podemos medir cambios de la fase en el VI con infarto no transmural?
Podemos medir cambios de la fase en el VI con tejido infartado?
Ejemplo de un paciente con Chagas y defecto de perfusión
Ejemplo de un paciente con Chagas y defecto de perfusión

Courtesy
Paola Smanio, MD
LV Remodeling in HF: Autopsy Examples

Normal                Systolic HF                Diastolic HF

Bonema et al. Chptr 2 in Klein and M. Garcia
Análisis de Fourier del Engrosamiento Sistólico y diastólico

By detecting the regional onset of mechanical relaxation
Chen et al, J Nucl Cardiol 2011, 18: 299-308
Paciente con Disincronía Diastólica pero no sistólica

ESRD 53 yo male: Chen et al, J Nucl Cardiol 2011, 18: 299-308
Disincronía Sistólica y Diastólica en pacientes con ESRD
Chen at al, J Nucl Cardiol 2011;18:299-308

Normal Controls vs ESRD Patients
Prevalence rates of systolic and Diastolic dyssynchrony in ESRD pts
Marcasposo BiVentricular = Terapia de Resincronización Cardiaca

Pulse generator houses the battery and a tiny computer.

Leads: Wires that send impulses from the pulse generator to the heart muscle, as well as sense the heart's electrical activity. Each impulse causes the heart to contract.

Left Ventricular Lead

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Cardiac Resynchronization Therapy (CRT) in Heart Failure

- CRT was approved by the FDA in 2001 based on the MUSTIC and the MIRACLE trials.
- In patients with end-stage HF, depressed LVEF and wide QRS (>120 ms).
- 20% to 30% of these patients do not respond to CRT.
- 30% of patients with a wide QRS complex (>120 ms) do not have substantial LV dyssynchrony on echocardiography.
- One third of patients with a narrow QRS appear to have substantial LV dyssynchrony on echocardiography.
- Results of the PROSPECT trial showed that TDI and myocardial strain-rate is not ready for routine clinical evaluation of LV dyssynchrony.
A female patient had class-III HF due to dilated cardiomyopathy and left bundle branch block. She improved to class-I HF after CRT.

<table>
<thead>
<tr>
<th></th>
<th>Phase SD</th>
<th>Bandwidth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre CRT</td>
<td>68.9°</td>
<td>211°</td>
</tr>
<tr>
<td></td>
<td>(*p&lt;0.0001)</td>
<td>(*p&lt;0.0001)</td>
</tr>
<tr>
<td>Post CRT</td>
<td>14.4°</td>
<td>46°</td>
</tr>
<tr>
<td></td>
<td>(*p=0.3085)</td>
<td>(*p=0.0543)</td>
</tr>
<tr>
<td>Normal Limits</td>
<td>11.8±5.2°</td>
<td>30.6±9.6°</td>
</tr>
</tbody>
</table>

*One-sample z test

Ami E. Iskandrian, MD, University of Alabama at Birmingham
Ejemplo de paciente antes y después de la resincronización biventricular

A. Phase histogram before CRT

B. Phase histogram after CRT

. Dynamic OMC displays of the patient before CRT

. Dynamic OMC displays of the patient after CRT
Cual paciente responderá a TRC?

Class III Heart Failure
LVEF (Echo) = 32%

Class III Heart Failure
LVEF (Echo) = 27%
Class III Heart Failure
LVEF (Echo) = 32%

Patient with LVEF < 35% but retaining LV synchrony = NO CRT
Class III Heart Failure
LVEF (Echo) = 27%
VI que no responde al TRC por no tener disincronía
Evaluación Clínica: Cuales Pacientes Responderan al Tratamiento de Resincronización Biventricular?

- LV dyssynchrony measured by phase analysis of gated SPECT MPI can be used to predict response to Cardiac Resynchronization Therapy (CRT) with sensitivity and specificity of 70% and 74% respectively.
- Henneman MM, Chen J, et al. JNM 2007; 48:1104-1111
Predicting response to CRT: Clinical considerations

- Patient in HF NYHA Class III or IV?
- LVEF < 35%?
- LV dyssynchronous?
  - QRS > 130 ms (electrically)
  - Mechanically (accurately and reproducibly)
- Is wall for lead placement viable?
  - Bleeker et al, Circulation 2006; 113:969-976
- Is LV lead placed at the latest viable mechanical activation site?
VI que no responde al TRC por tener tejido infartado
Técnica avanzada para medir el tejido infartado
Correlación entre LGE-MRI y SPECT IPM de medir la carga del VI necrosis (scar burden)

* Apex not assessed by MRI
Correlación entre LGE-MRI y SPECT IPM de medir la carga del VI necrosis (scar burden)
Colocación óptima del electrodo VI de TRC en la última región de engrosamiento

Concordant lead: 6 mo
ΔESV 139 ml → 86 ml
Δ EF 32% → 44%

Disoncordant lead: 6 mo
ΔESV 124 ml → 153 ml
Δ EF 27% → 22%

52 concordant / 38 discordant

Ejemplo de fusión de SPECT y Venograma de TAC

A. CT volumetric display

B. Fusion display

Slide courtesy of Ji Chen PhD
Análisis de la Fase en la Disincronía Cardiaca

- Está implementado en el software de ECTb, QGS, y 4DM.
- El procedimiento es automático y se puede aplicar a estudios antes adquiridos.
- Se puede medir con 8 o 16 cuadros por ciclos cardiacos.
- Se puede medir en regiones de cuentas disminuidas.
- Se ha determinado que es preciso y reproducible en medir PSD y PHB.
- Usa sincronicidad, viabilidad, y el último segmento en engrosarse para ayudar a guiar la terapia TRC.
- Ensayo de 21 centros en China (GuideCRT)
Cardiac dyssynchrony: We have the tools. It is time to use them

Steven Port, MD


It has now been over a decade since the appearance of the first clinical report demonstrating improvement in symptoms after cardiac resynchronization therapy (CRT).1 CRT was initially applied to patients with depressed left ventricular systolic function, severe congestive heart failure (CHF) and a wide QRS on the electrocardiogram. Much has been learned since then.

As additional reports filtered in, it became apparent that not only did symptoms improve but also measurable changes in left ventricular volumes, i.e., reverse remodeling, increases in left ventricular ejection fraction (LVEF), reduction in the severity of mitral regurgitation, decreases in the occurrence of severe heart failure, and most notably, improved survival were documented.2-5

of improvement after CRT varies considerably. Many authors quote an approximate 65%-70% improvement rate with the widely held notion that fully 1/3 of patients do not experience any benefit. The truth may not even be that good because, benefit has typically included quality of life measures assessed by either or both patient and physician and physicians may not be easily blinded to the therapy due to the knowledge of the lead insertion or to the

From the Aurora Cardiovascular Services, Aurora Health Care, Milwaukee, WI
Reprint requests: Steven Port, MD, Aurora Cardiovascular Services, Aurora Health Care, Milwaukee, WI; sport@wi.rr.com.
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doi:10.1007/s12350-012-9526-9

Published online: 24 February 2012
Gracias
Calculation of Peak Velocity Difference by Tissue Doppler Imaging

FIGURE 1. Calculation of the PVD. (A) In the apical 4-chamber view, the time from the onset of the QRS to peak velocity is determined and recorded for the septal (yellow) and lateral (green) regions. (B) In the apical 2-chamber view, the times from the onset of the QRS to the peak in the inferior (yellow) and anterior (green) regions are recorded. (C) In the apical 3-chamber view, the times from the onset of the QRS to the peak of the posterior (yellow) and anteroseptal (green) regions are recorded. (D) Once the 6 measurements are obtained, the smallest time to peak is subtracted from the largest time to peak, giving the PVD.

<table>
<thead>
<tr>
<th>Metric</th>
<th>Time (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septal to peak</td>
<td>460</td>
</tr>
<tr>
<td>Lateral to peak</td>
<td>220</td>
</tr>
<tr>
<td>Inferior to peak</td>
<td>460</td>
</tr>
<tr>
<td>Anterior to peak</td>
<td>220</td>
</tr>
<tr>
<td>Posterior to peak</td>
<td>450</td>
</tr>
<tr>
<td>Anteroseptal to peak</td>
<td>200</td>
</tr>
<tr>
<td>PVD</td>
<td>260</td>
</tr>
</tbody>
</table>
Efectos de resincronización por Marcapaso BiVentricular

Kerwin et al. JACC 2000, 5:1221-1227
Evaluación de la asincronía ventricular en la insuficiencia cardiaca por análisis de la fase: Usando IPM-sincronizadas

- Es un software que procesa automáticamente y se puede aplicar a estudios previos.
- Predice que paciente responderá al tratamiento de resincronización cardiaca.
- Puede evaluar el valor del tratamiento en pacientes específicos.
Would 16 frames/cycle yield higher temporal resolution than 8 for a typical clinical study?

• No, cts/frame are more important than # frames/cycle
  – 16 frames better only if study acquired for 2X time of 8 frame study
  – Chen et al, J Nucl Cardiol 2008; 15: 383-391