Use of Dual Energy CT (DE-CT) in myocardial perfusion alterations detection.

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Learning objectives

Describe the possible myocardial perfusion alterations that can be revealed with a cardiac CT in Dual-Energy modality (DE):

- Ischemic perfusion defects highlighted in stress conditions and reversible in rest conditions

- Fixed ischemic perfusion defects (necrosis-fibrosis areas)

- Perfusion alterations based on non-ischemic causes
Background

The most common cause of myocardial perfusion alterations is the ischemic pathology. However other pathologies such as infective myocarditis and cardiomyopathies (genetic, toxic-metabolic, idiopathic) can also determine perfusion alterations with a non-ischemic distribution pattern.

The most frequently employed imaging modalities for myocardial perfusion evaluation are SPECT, PET and MRI. The latest allows myocardial tissue characterization with high contrast resolution. Up to today CT is the most accurate examination for non-invasive assessment of coronary atherosclerosis, however, based on anatomic-morphological characteristics only, it's not possible to determine the physiopathological meaning of a coronary atherosclerotic plaque. As shown in studies with invasive measurement of the coronary fractional flow reserve obtained during coronaryography [1], the downstream perfusion alteration of an intermediate coronary stenosis (40-70% of lumen restriction) can be uncertain.

For these reasons, in clinical practice, morphological informations regarding coronary arteries acquired with coronary-CT are often integrated with a functional imaging examination, such as ECHO-stress, SPECT, PET or MRI. The functional data are essential in the diagnostic-therapeutic management of the patient.

DE CT allows to determine the iodine distribution during the contrast agent first pass, based on the known absorption characteristics of this element at different kV. Different kV can be obtained: 1) with second generation dual-source CT scans in Dual-Energy modality or 2) with single tube CT scans by means of quick switching of X-rays emissions at different kV. A stress CT examination performed after an hyperemic pharmacological stimulation (Adenosine, Dipyridamole) can offer an important contribution and help to interpret more exhaustively the examination.
Findings and procedure details

EXAMINATION TECHNIQUE

In our case series examinations have been acquired with a second generation dual-source 128 slice CT scan (Somatom Definition Flash, Siemens, Erlangen, Germania).

Suspicion of ischemic cardiomyopathy

Whenever the study is performed for a suspicion of CAD, the protocol includes several acquisitions. After the patient has been elucidated regarding the procedure and an informed consent has been obtained, a pre-contrast scan is acquired (Calcium Score) in order to plan the exact range for the following steps. A vasodilator drug able to induce myocardial ischemia is administered for the successive acquisition in stress condition. The most frequently used vasodilator agents, both in our case series and in the literature, are Adenosine and Dipyridamole. The first one acts directly on adenosine receptors, while the second elevates Adenosine endogenous levels by reducing its uptake from endothelial cells. These drugs, dilating the resistance coronary arterioles, tend to abolish the auto-regulation mechanism ("transmural coronary steal") with a subsequent flow reduction downstream the stenosis that is more severe as the stenosis increases. Both have demonstrated a good sensibility and specificity but Dipyridamole has the advantage to be a lot cheaper and has a more prolonged effect (some minutes respect to the few seconds of Adenosine). Both can be safely administered with contraindications in patients with asthma, COPD or high grade AV-block without an implanted pace-maker. The drug is injected based on body weight with an infusion pump. The dose is 0.14 mg/kg/min in 3-5 minutes for Adenosine or of 0.56 mg/kg (low dose) - 0.84 mg/Kg (high dose) in 4-6 minutes for Dipyridamole. Before the examination the patient cannot ingest methylate xanthines such as coffee, tea, chocolate, energetic beverages or assume bronchodilator drugs that antagonize the effect of the medications used during the examinations.

To inject the drugs and the contrast agent two venous accesses are obtained. During the examination a 12 derivations electrocardiogram, blood pressure and oxygen saturation are constantly monitored. The CT scan room setting is shown in Fig. 1 on page 8. The patient is questioned several times for the appearence of symptoms like nausea, vertigo, headache, thoracic pain and general malaise. These manifestations usually disappear when the drug is suspended or with the administration of an antagonist (Aminophylline 120-240 mg e.v.). At the end of the infusion the first acquisition in stress conditions with the DE modality (100/140 kV) with retrospective ECG-triggering (with prospective ECG-based tube current modulation) is performed. The administration of contrast agent (#70 ml of contrast media followed by 50 ml of physiological solution at 5 mL/sec) is temporized based on bolus-triggering with a ROI in the ascending aorta. When the stress...
scan is completed, in case it's needed, the antidote is administered (Aminophylline). After a 15-20 minutes break, necessary for a complete myocardial wash-out of the contrast agent previously injected and for a complete resolution of the pharmacological effect, an acquisition in rest conditions is performed for a combined evaluation of coronary arteries and myocardial perfusion at rest, generally with a prospectively ECG-triggered scan or with a prospective high pitch spiral can (which is possible in second generation dual-source CT scans) to reduce the radiation dose. If the heart rate is deemed too high, some beta-blockers can be administered. An optional sequence can be added at 8-10 minutes, without further contrast agent injection, to reveal the presence of late-enhancement areas indicative for necrotic-fibrotic zones; it's preferable to use low kV protocols (80-100 kV) that enable not only to reduce the radiation dose but also to highlight the difference between vital and ischemic myocardium [3].

EXAMINATION PROTOCOLS

- Suspicion of ischemic cardiomyopathy

It's important to optimize the timing of the acquisition in stress conditions during contrast agent first pass after its administration in order to catch the myocardium peak enhancement and optimize the assessment of ischemic areas respect to normally perfused remote myocardium. A temporal window ranging from 24 to 32 seconds after contrast administration has recently been described as the best to reveal the maximum attenuation difference between vital and pathological myocardium [3]. Different acquisition protocols have been proposed in the literature. Meinel et al [4] have addressed this issue in a recent study confronting the accuracy of different acquisition protocols with DE modality respect to SPECT examinations in stress/rest: the protocol including a double DE scan in pharmacological stress and rest conditions should be chosen in order to identify fixed or reversible perfusion defects with a 99% sensibility, 97% specificity, 92% positive predictive value and 100% negative predictive value; the acquisition to determine the presence of late-enhancement areas wasn't shown to improve diagnostic accuracy.

The examination protocols can be the following:

1. An acquisition after pharmacological stress with a subsequent acquisition in rest condition (Fig. 2 on page 8)

2. An acquisition at rest followed by an acquisition under pharmacological stress (Fig. 3 on page 9)
Both protocols present some advantages and some disadvantages (Fig. 2 on page 8, Fig. 3 on page 9) [2,3]:

1. With the first protocol there is a higher sensibility in the scan in stress conditions and therefore in the identification of inducible ischemia. However the contrast agent remained after the first scan could partially contaminate the second scan in rest conditions reducing its sensibility in infarct areas identification (Fig. 4 on page 10; Fig. 5 on page 11; Fig. 6 on page 12).

2. In the second case there is a higher sensibility and therefore a higher accuracy in the identification of infarct areas. However, the contrast agent remained after the first scan could partially contaminate the second scan in stress condition reducing its sensibility in the identification of inducible ischemia. These can be underestimated also because of beta-blockers employment for the first scan. The advantage of this approach is that if no significant stenosis are identified the examination can be interrupted with radiation dose and contrast media reduction for the patient.

- **Suspicion of non-ischemic cardiomyopathy**

Cardiomyopathies with various non-ischemic etiologies can determine perfusion alterations that can be revealed with DE CT, for example myocarditis [5]. In this case the optimal timing for images acquisition has still to be defined. In our case series performing acquisitions 5-7 minutes after contrast administration, it was possible to identify hyperdense areas with characteristics analogous to those that can be identified in MR late enhancement sequences: non-ischemic pattern (independent from coronary distribution), often with epicardial distribution in the lateral/infero-lateral left ventricle wall, and associated with hyperemic thickening of the pericardium (Fig. 7 on page 13; Fig. 8 on page 14; Fig. 9 on page 15; Fig. 10 on page 16).

**POST PROCESSING AND IMAGES INTERPRETATION**

Acquired images are elaborated with a dedicated software for a combined evaluation of coronary anatomy and myocardial perfusion.

From raw data it's possible to obtain axial reconstructions from the two tubes at different kV (100 e 140 kV) and fusion images with contributions from the two datasets that can be equal (50%-50%) or up to 70-30% respectively for the 140 kV and 100kV tubes with a dedicated convolution kernel (D30f Siemens). The thus created fusion dataset combines the reduced noise of the high energy level (140 kV) and the high contrast resolution of the low energy level (100 kV) to obtain a better definition between normally perfused and hypoperfused myocardium [6]. A myocardial iodine distribution map is therefore
created, represented with a color encoding and superimposed on the virtual pre-contrast reconstruction (VNC= virtual non contrast) [6]. Images can be evaluated with a visual qualitative scale and/or by means of ROIs positioned in the areas to be studied. In the second case iodine distribution data (expressed in \( \text{mg/mL} \)) are normalized based on the remote myocardium or ventricular cavity.

Colorimetric maps represent the myocardial static distribution of the contrast agent in the exact moment of the image acquisition [6]. During first pass early arterial phase myocardial areas with reduced vascularization have a lower iodine content and therefore appear as hypodense. These areas are defined as perfusion defects and indicate infarct or inducible ischemic defects (Fig. 11 on page 17). If the hypodense zone is visible only in stress acquisitions, it's indicative of myocardial ischemia; if the area remains hypodense also during rest acquisition, it's an infarct (Fig. 11 on page 17) [7].

Iodine based contrast agents, as those based on Gd, accumulate in the irreversibly damaged myocardiocytes intracellular space in case of acute myocardial infarction or in the expanded extracellular space in the event of fibrous scar: these necrotic/fibrotic areas can therefore be revealed as hyperdense zones (iperenhancement) at a late scan 10-15 minutes after contrast agent injection (Fig. 10 on page 16) [8].

**DOSE AND ACCURACY**

According to the literature, the radiation dose delivered for a single Dual-Energy acquisition ranges between 5.7 and 7.7 mSv [6,9] (Fig. 12 on page 18). However, in our experience, with prospective ECG-based tube current modulation (MinDose, Siemens), it's often possible to keep the dose under 5 mSv. Based on these data this technique appears very competitive respect to SPECT examinations (dose= about 10mSv for 99mTc and 20-40 mSv for 201 TI) [10, 11], considering that it also has the advantage to combine in a single study both anatomical and functional data.

Regarding diagnostic accuracy in stress/rest perfusion evaluation, preliminary data are very favorable (Fig. 12 on page 18) since the technique presents good sensibility and specificity (%90%) respect to SPECT, MRI and invasive quantitative coronarography [4, 8, 9, 12, 13]. Ko et al have studied the added value of perfusion assessment with DE modality in stress and rest conditions, by comparison with invasive coronarography in the identification of ischemic areas: sensibility, specificity, PPV, NPV and ROC curves were significantly better for CT perfusion then for coronaro-CT only [9].
Images for this section:

**CT scan room setting**

- Double venous access (vasodilator agent and contrast agent administration)
- Infusion pump
- Blood pressure, O$_2$ saturation and 12-leads ECG continuous monitoring
- Continuous clinical monitoring

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**Fig. 1**

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Stress➔Rest protocol

- Adenosine / Dipyridamole infusion
- Calcium Score
- Stress CCT 3-4 min
- 15-20 min
- Rest CCT
- Delayed CCT (optional) 8 min
- Contrast (50cc) 60cc

- IV Access
- 12-Lead ECG
- Vital

- t [min] 20-40 min

▪ Stress➔Rest: more sensitive for detecting ischemia
▪ Target population: high pre-test probability of CAD or patients with known CAD

Fig. 2

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Fig. 3

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CASE 1

M, 50 y/o
- Atypical pain
- Known CAD, previous PCI on LAD and main OM branch

![Diagram of heart with text boxes for Preparation, Topogram, Testbolus, Stress Myocardial Perfusion Dual-Energy, Rest Coronary Anatomy + Perfusion Dual-Energy, Dipyridamole (0.56 mg/kg over 4 min), Contrast 50 mL, and Contrast 60 mL.]

Fig. 4

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Fig. 5

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Fig. 6

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CASE 2

♀ 66 y/o
- Previous surgery, RT and CT for breast cancer
- Atypical pain and rest dyspnea at rest
- Hospitalization at the Emergency Department for dyspnea and diarrhea
- TnT: 24.6 mg/L; elevated RCP; AV block
- Echocardiography: DCM (EF=30%) with accidental finding of left ventricle apex formation (thrombus?)

Fig. 7

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CASE 2

The first scan revealed an apical thrombus in the left ventricle (A) (confirmed also with MRI (B)) and excluded the presence of significative coronary stenosis (C, D, E, F, G).

Agatston score = 128.2

Fig. 8

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CASE 2
Biventricular function severely compromised

LV EF = 33%
RV EF = 36%

Fig. 9

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Fig. 10

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Fig. 11

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Table 1: summary of the most relevant studies regarding cardiac perfusion CT with Dual-Energy technique

<table>
<thead>
<tr>
<th>Author</th>
<th>Year / No. pts</th>
<th>CT Protocol</th>
<th>CT Scanner</th>
<th>Stressor</th>
<th>Dose (mSv)</th>
<th>Analysis</th>
<th>Reference</th>
<th>SE (%)</th>
<th>SP (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ko et al.</td>
<td>2011 / 41</td>
<td>1. Rest Retro 2. Stress Dual-Energy</td>
<td>1° Dual-Source</td>
<td>Adenosine (140μg/kg/min)</td>
<td>5.8 (K=0.017)</td>
<td>Iodine map</td>
<td>QCA and MRI 1.5 T</td>
<td>89</td>
<td>78</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Ko et al.</td>
<td>2012 / 45</td>
<td>1. Rest Retro 2. Stress Dual-Energy</td>
<td>1° Dual-Source</td>
<td>Adenosine (140μg/kg/min)</td>
<td>5.7 (K=0.017)</td>
<td>Iodine map</td>
<td>QCA</td>
<td>89</td>
<td>74</td>
<td>80</td>
<td>85</td>
</tr>
<tr>
<td>Meinel et al.</td>
<td>2013 / 55</td>
<td>1. Rest Dual-Energy 2. Stress-Dual-Energy</td>
<td>2° Dual-Source</td>
<td>Adenosine (140μg/kg/min) Regadenoson (0.4 mg)</td>
<td>7.1 (K=0.014)</td>
<td>Iodine map</td>
<td>SPECT</td>
<td>99</td>
<td>97</td>
<td>92</td>
<td>100</td>
</tr>
<tr>
<td>Kido et al.</td>
<td>2014 / 21</td>
<td>1. Stress-Dual-Energy</td>
<td>1° and 2° Dual-Source</td>
<td>Adenosine (160μg/kg/min)</td>
<td>7.7</td>
<td>Iodine map</td>
<td>QCA</td>
<td>67</td>
<td>92</td>
<td>84</td>
<td>82</td>
</tr>
<tr>
<td>Kim et al.</td>
<td>2014 / 50</td>
<td>1. Stress-Dual-Energy 2. Rest Retro</td>
<td>2° Dual-Source</td>
<td>Adenosine (140μg/kg/min)</td>
<td>6.5 (K=0.014)</td>
<td>Iodine map</td>
<td>MRI 1.5 T</td>
<td>77</td>
<td>94</td>
<td>53</td>
<td>98</td>
</tr>
</tbody>
</table>

Fig. 12

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Conclusion

Cardiac DE CT allows to evaluate in the same examination and with limited radiation dose, both the coronary arteries and the areas of altered myocardial perfusion.
References


