Incontri Bresciani di Radioterapia Oncologica – Edizione 2014
Brescia Meetings in Radiation Oncology – 2014 Edition

NORTHWEST PASSAGE:
KEY-FUNCTIONS PRESERVATION
IN ONCOLOGY

Brescia – September 25th/26th, 2014

Imaging of cardio-pulmonary treatment related damage

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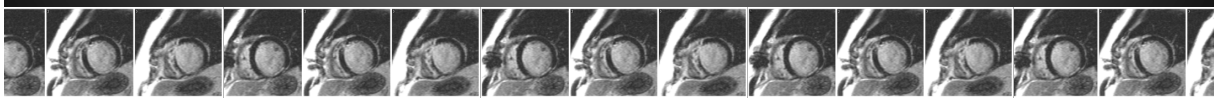
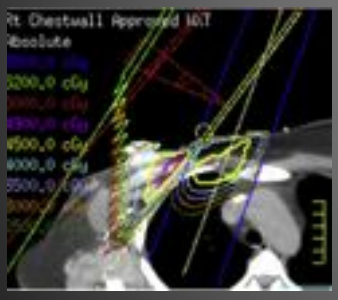
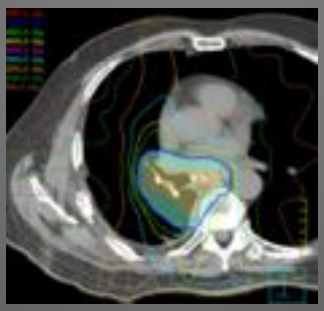


Radiotheraphy and Lung

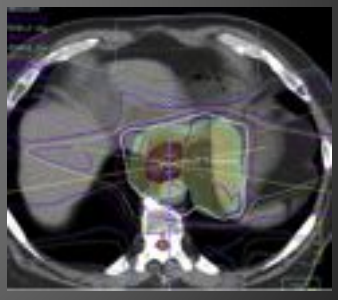
- The goal of radiation therapy (RT) is to reduce or eliminate the tumor with minimal toxicity to normal surrounding tissue
- RT is used to treat many intrathoracic and chest wall malignacies (breast cancer, bronchogenic carcinoma, oesophageal neoplasm, malignant mesothelioma and lymphoma)



Brest cancer→ 3D-CRT



NSCLC→ IMRT



Oesophageal cancer → IMRT

Benveniste MFK et al Clinical Radiol;2013; Graves PR et al Semin Radiat Oncol 2010

Radiation-induced lung injury (RILD)

- The lung is one of the most sensitive tissue to ionizing radiation and damage to normal lung tissue remains the main obstacle in RT
- Radiation-induced lung disease (RIDL) is a frequent complication of RT *(40% of patients develop radiographic abnormalities - 7% develop symptomatic pneumonitis)*
- Radiation-induced changes in the lung are dependent on a number of factors inclundig:
  - *Patient-specific factors (age, smoking, pre-exsting lung disease)*
  - *RT technique (3D CRT, IMRT e SBRT)*
  - *Radiation dose*
  - *Volume of lung irradiated*
  - *Administration of chemotherapy*

Benveniste MFK et al Clinical Radiol 2013; Graves PR et al Semin Radiat Oncol 2010
Mesurolle B et al Radiographics 2000; Park et al Radiographics 2000; Jennings FLAA 1962

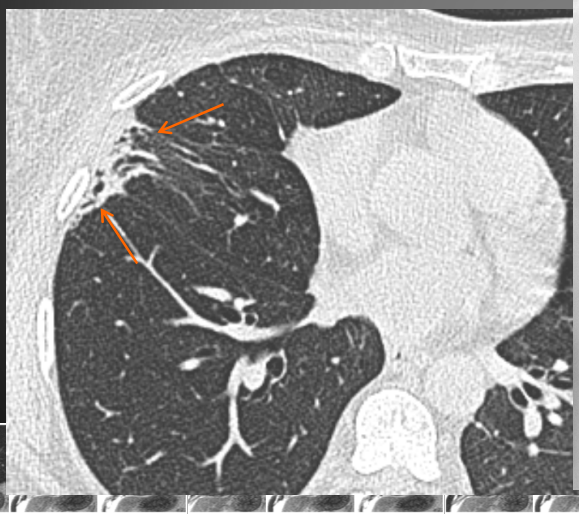
Radiation-induced lung disease (RILD)

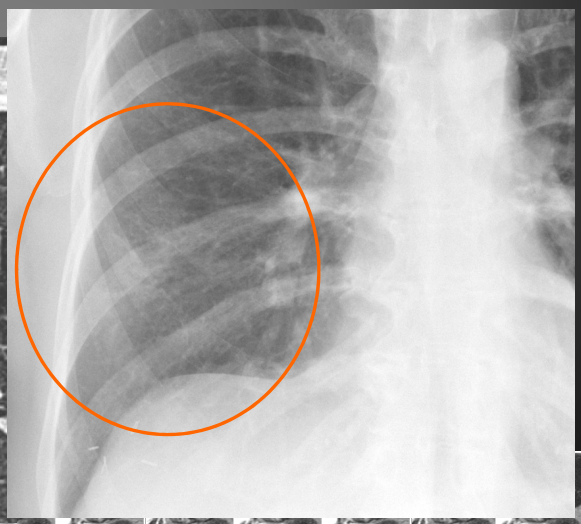
- Two distinct clinical, pathologic,and radiologic phases of RILD are recognized:
  - Acute phase (*Radiation Pneumonitis → 4-12 weeks after RT)*
  - *Chronic phase (Radiation Fibrosis → several months after RT)*
- Depending on the severity of lung injury, these abnormalities may resolve completely, but they more often undergo progressive organization and eventually lead to fibrosis

Benveniste MFK et al Clinical Radiol 2013; Park et al Radiographics 2000;
Larici AR et al Radiographics 2011

Usual Radiologic Findings after RT

- RILD is not generally seen with doses below 20Gy and it is most commonly seen with doses > 40Gy.
- Radiologic manifestations of RILD, generally confined to the field of irradiation, are *better detected on CT* than chest radiographs

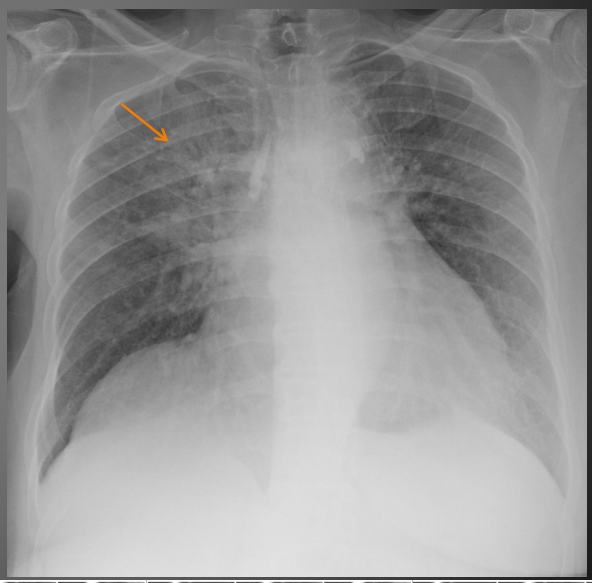




Usual Radiologic Findings after RT

- Acute phase (Radiation Pneumonitis)

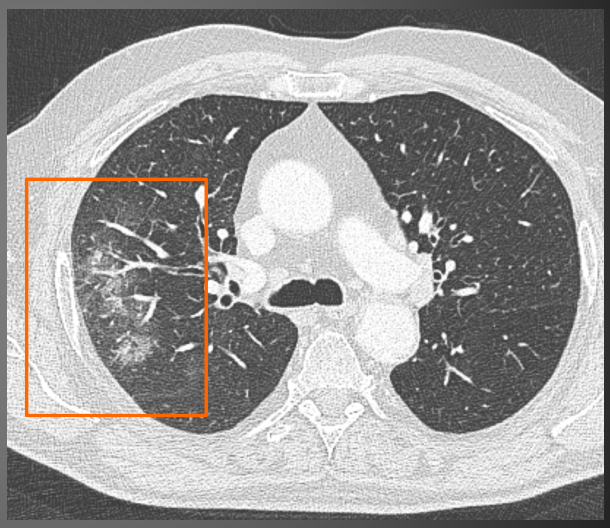
- Chest X-ray
  - Diffuse haziness
  - Consolidation
  - Pleural effusion
  - Elevation of diaphragm



Usual Radiologic Findings after RT

- Acute phase (Radiation Pneumonitis)

- CT (more sensitive)
  - Ground-glass opacity
  - Patchy or dense consolidation
  - Pleural effusion

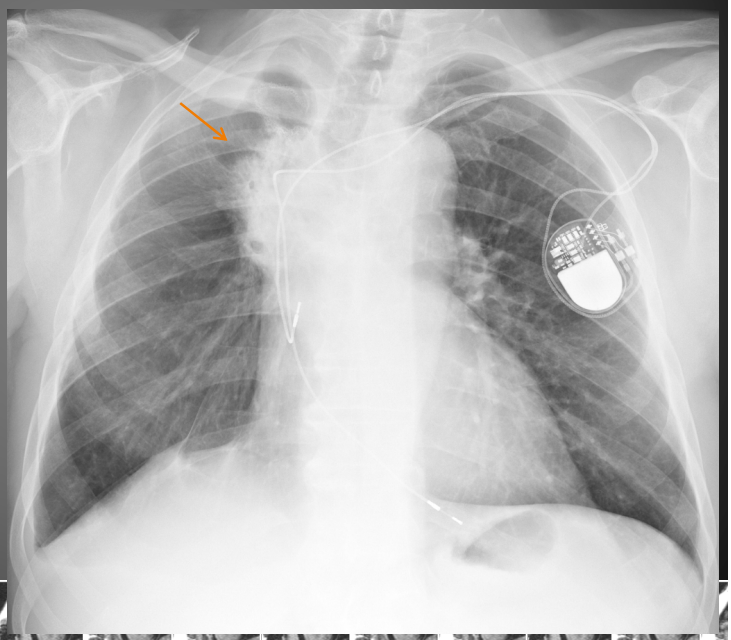


Benveniste MFK et al Clinical Radiol 2013;

Usual Radiologic Findings after RT

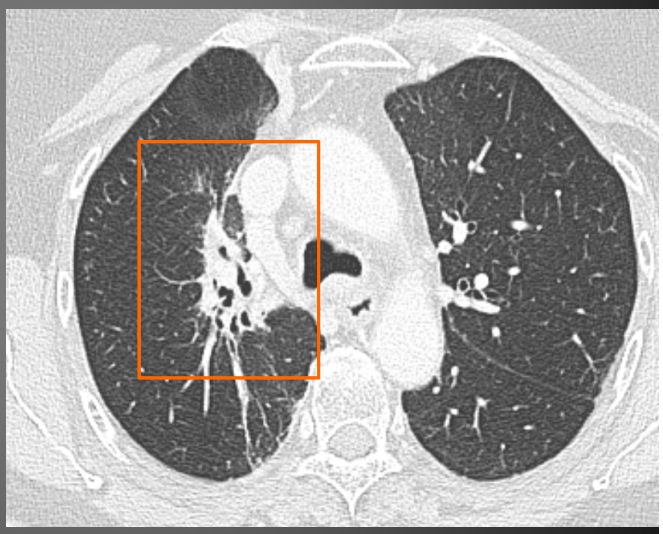
- Chronic phase (Radiation Fibrosis)

- Chest X-ray
  - Linear opacities
  - Dense consolidation
  - Architectural distortion
  - Volume loss
  - Shift of the mediastinum
  - Elevation of diaphragm



Usual Radiologic Findings after RT

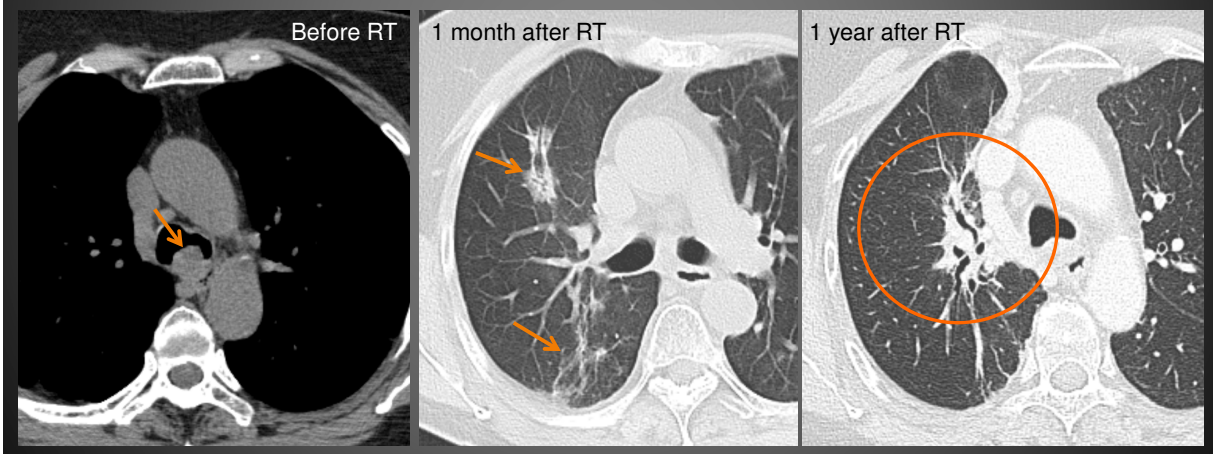
- Chronic phase (Radiation Fibrosis)
- CT (more sensitive)
  - Steaky opacities
  - Dense consolidation
  - Traction bronchiectasis
  - Architectural distortion
  - Volume loss
  - Pleural thickening
  - Shift of the mediastinum
  - Elevation of diaphragm



Benveniste MFK et al Clinical Radiol 2013; Graves PR et al Semin Radiat Oncol 2010

Usual Radiologic Findings after RT

- Acute and chronic phase
  - 53 year-old female with mucoepidermoid carcinoma of the tracheal carina



Unusual Radiologic Findings after RT

Target Organ	Complication	Time to Onset	Fractionated Dose	Reference
Lung	Pneumonitis	1–3 mo (acute), 12–15 mo (late)	30 Gy	Mosvas et al (3)
	Necrosis	12 mo (1–7 y for cavitations)	>60 Gy	…
	BOOP*	6 wk to 10 mo	Breast carcinoma irradiation; no minimal dose defined	Crestani et al (4)
	Pneumothorax	16 mo	>30 Gy	Penniment and O'Brien (5)

- Necrosis: uncommon (0.6%), severe and late complication after RT (>60 Gy)
- Cavitation within the radiation fibrosis may also indicate an infectious process (including TBC) and recurrent tumour

Mesurolle B et al Radiographics 2000

Unusual Radiologic Findings after RT

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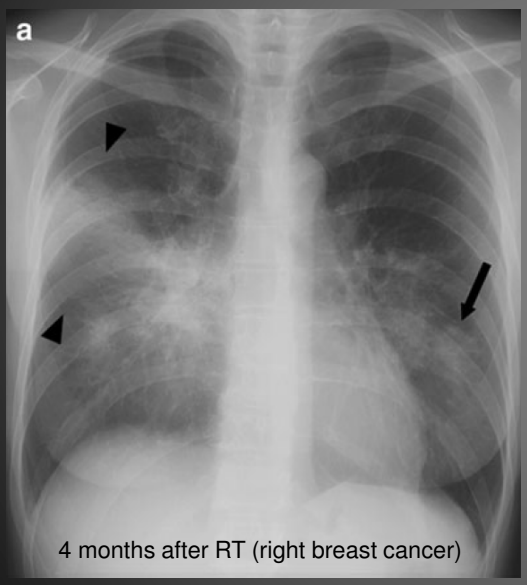
- Pneumothorax (1%): usually occurs in patients with radiologic evidence of post-irradiation fibrosis
- BOOP (2.5%): patchy, bilateral and multifocal migratory lung opacities (consolidation and ground glass infiltration)

Mesurolle B et al Radiographics 2000; Kano et al. Jpn J Radiol 2012

Unusual Radiologic Findings after RT

- BOOP: patchy, bilateral and multifocal migratory lung opacities (consolidation and ground glass infiltration)



4 months after RT (right breast cancer)

Kano et al. Jpn J Radiol 2012

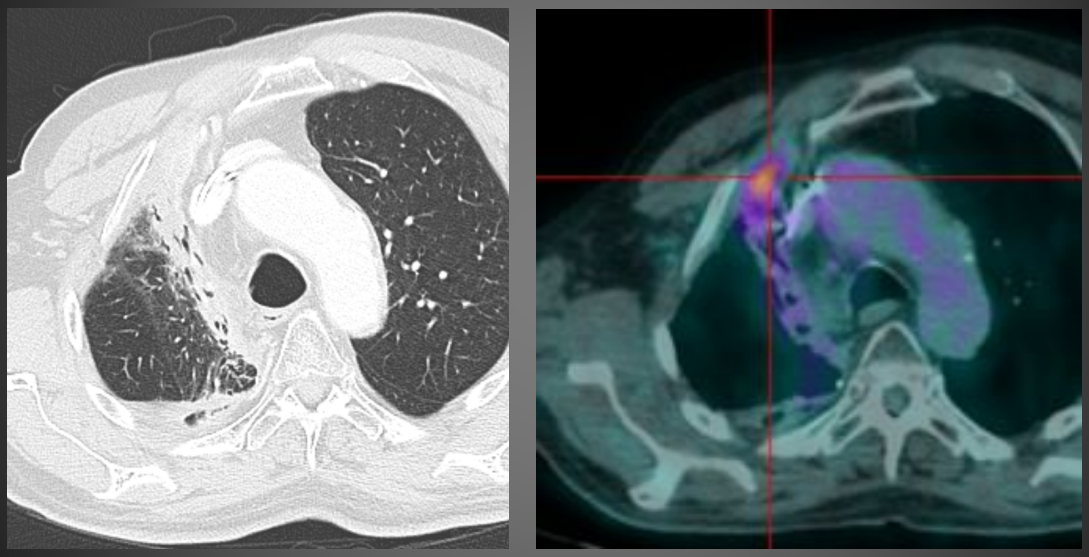
Differential diagnosis considerations

- When radiological manifestations of radiation damage are different from the expected patterns, other disease entities have to be considered
  - Infection
    - *Before completion of RT*
    - *Abrupt onset*
    - *Lung opacities outside of the treated areas*
    - *Tree in bud pattern*
  - *Recurrent tumor*
    - *Occurs within 2 years after RT is completed*
    - *Development of a lobulate contour within the fibrosis*
    - *PET-CT improved DD between recurrent tumour and radiation fibrosis (**PET-CT is best performed 6 months after RT is completed)*

Benveniste MFK et al Clinical Radiol 2013; Munden RF et al Radiation-induced lung disease. 1st ed. Philadelphia: Saunders-Elsevier; 2008.

Recurrent tumor within fibrosis PET-TC

recurrent tumor 18 months after RT



Focal FDG uptake is suggestive of residual or recurrent disease

Conclusions

- RT is an important modality in the treatment of patients with neoplasms.
- Knowledge of pulmonary abnormalities related to RT is important to recognize patterns of RILD and detect complications, such as recurrent malignancy or infection.

Benveniste MFK et al Clinical Radiol;2013; Graves PR et al Semin Radiat Oncol 2010;
Park et al Radiographics 2000; Mesurolle B et al Radiographics 2000;

Heart and RT: epidemiology

- Cardiovascular disease is now the most common non-malignancy cause of death in radiation-treated cancer survivors (Hodgkin's lymphoma and breast cancer), most often occurring decades after treatment (3 to 29 years after treatment).
- The long-term effects on the heart still remain unclear, mandating longer follow-up.
- Increased risk of coronary artery disease (CAD), congestive heart failure, valvular heart disease, pericardial disease, and sudden death.

Aleman BM et al. J Clin Oncol 2003;21:3431–9. Ng AK. Br J Haematol 2011;154:23–31.
Hoppe RT. Ann Oncol 1997; Suppl 1:115–8. Patnaik JL et al. Breast Cancer Res 2011;13:R64.

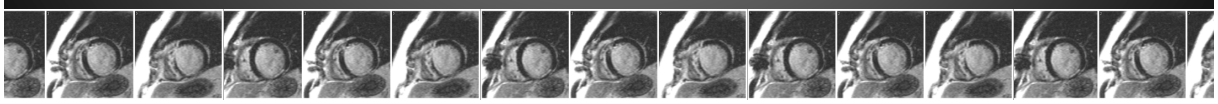
Table 2 Effects of Radiation Therapy on the Heart

Vascular
Coronary artery disease
Microvascular dysfunction
Structural
Valvular heart disease
Mitral stenosis and insufficiency
Aortic stenosis and insufficiency
Pericardial disease
Conduction system disease
Myocardial
Systolic dysfunction/systolic heart failure
Diastolic dysfunction/heart failure with preserved ejection fraction
Restrictive cardiomyopathy
Myocardial fibrosis/scar

Jaworski et al. JACC Vol. 61, No. 23, 2013

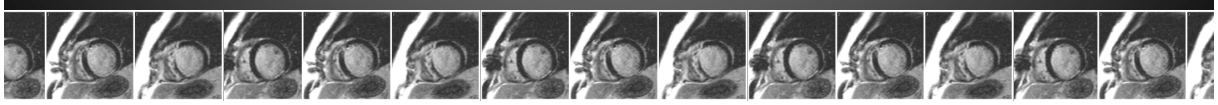
Prevention and follow-up

- Before radiotherapy: comprehensive baseline evaluation including a detailed cardiovascular history, cardiac examination, risk factor profiling, and echocardiography (systolic and diastolic function).
- Prolonged cardiological follow-up and cardiac screening is mandatory in cancer patients who have received irradiation to facilitate early identification of cardiac related complications.
- Control and minimize cardiac risk factors



Prevention and follow-up

- There is a paucity of data to support the optimal method and frequency of screening post-radiotherapy patients
- Development of a uniform approach to be potentially beneficial
- The focus of screening should ideally incorporate non-invasive, radiation-free modalities in the first instance



Cardiac imaging

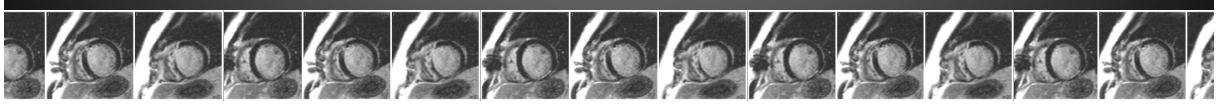
- Rest and stress echocardiography
- Cardiac magnetic resonance imaging (CMRI)
- Coronary computerized topography (CCT)

Structure	Abnormality	Natural History	Pathology
Pericardium	Pericarditis	Chronic asymptomatic effusion and/or pericarditis with symptoms: hemodynamic compromise with either constriction or tamponade	Fibrous thickening and fluid production
Myocardium	Myocarditis	Progressive diastolic dysfunction and restrictive hemodynamics with symptoms: CHF	Diffuse interstitial fibrosis/ microcirculatory damage leading to capillary obstruction/extensive fibrosis
Endocardium	Valvular damage	Over time, progressive stenosis and regurgitation	Cusp and/or leaflet fibrosis
Vascular System	Arteritis	Premature CAD/accelerated atherosclerosis Pulmonary hypertension	Ostial and proximal stenosis: LAD, RCA, and left main more than left circumflex Pathology similar to atherosclerosis
Conduction System		All forms of heart block and conduction delay	Fibrosis of conduction system
Autonomic Dysfunction		Supraventricular tachycardia; heart rate variability	

Feng M et al. Int J Radiat Oncol Biol Phys. 2011 January 1; 79(1): 10–18.

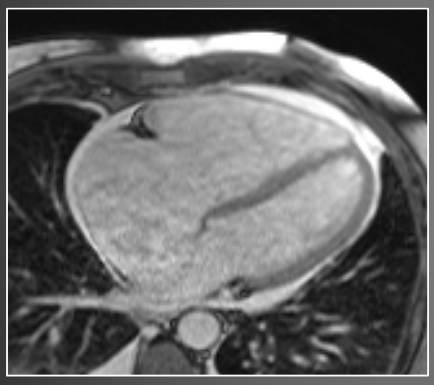
CMRI: sequences

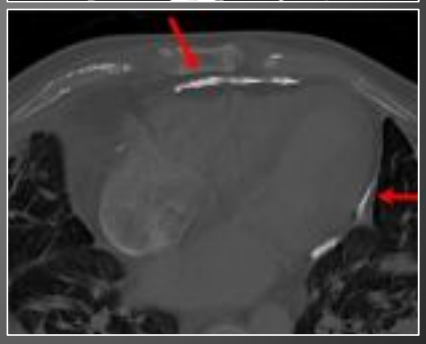
- Morfology
  black blood (HASTE, TSE T1, STIR T2)
  bright blood (True FISP)
- Function
  cine SSFP, Gradient-Echo
- Tissue characterization (delayed enhancement)
  segmented IR fast GE
- Perfusion
- Valvular Flow
  phase contrast

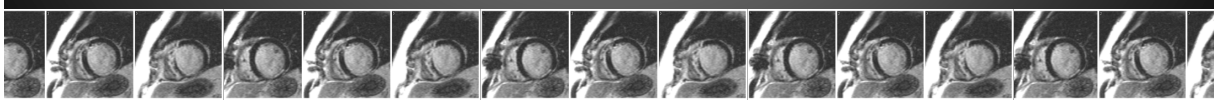


Morfology: acute and chronic pericarditis

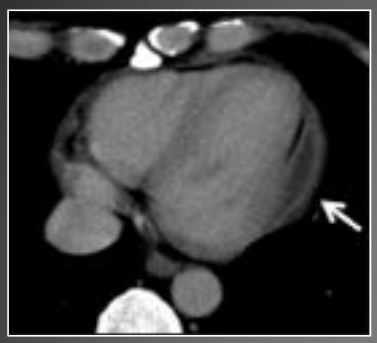
black blood (HASTE, TSE T1, STIR T2)
bright blood (True FISP)

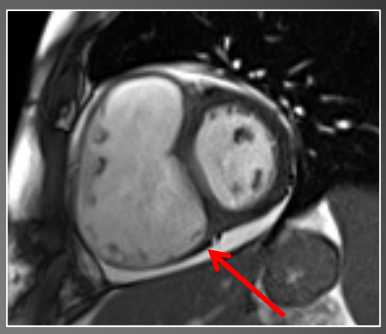


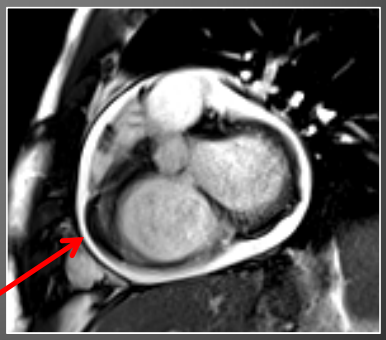


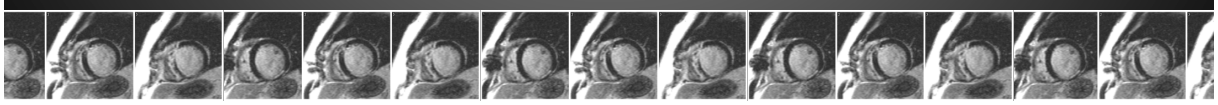


Morfology: acute and chronic pericarditis



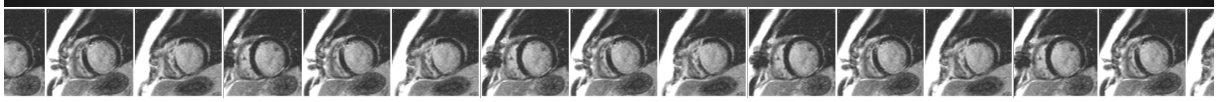






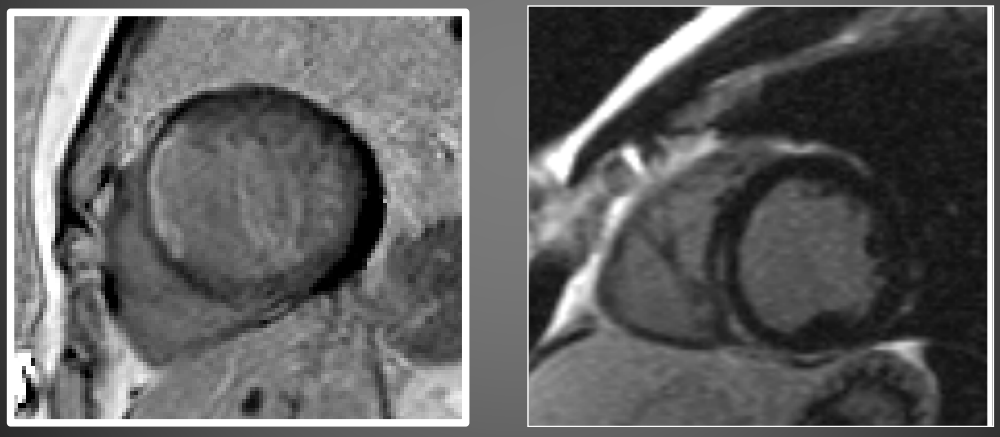
Tissue Characterization: edema and inflammation

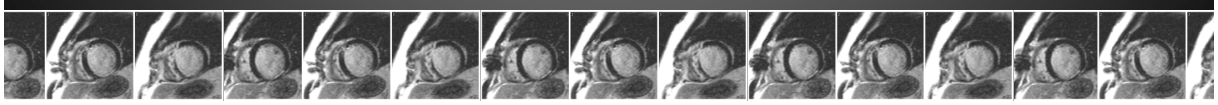
- Myocarditis: STIR T2 sequence



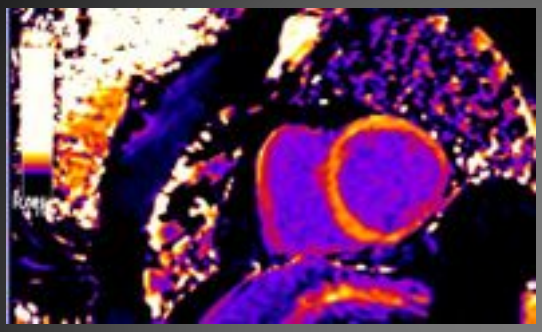
Tissue Caracterization: scar

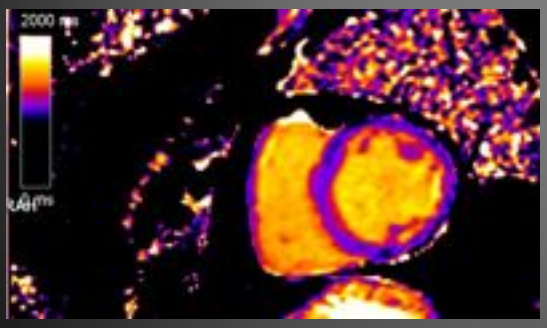
- Delayed enhancement
  segmented IR fast GE - PSIR





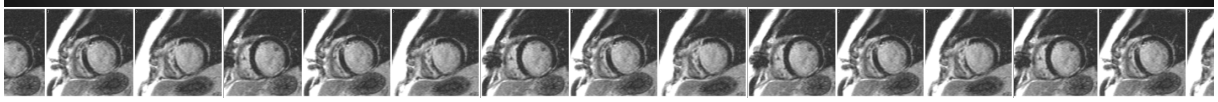
Tissue characterization: T1 mapping





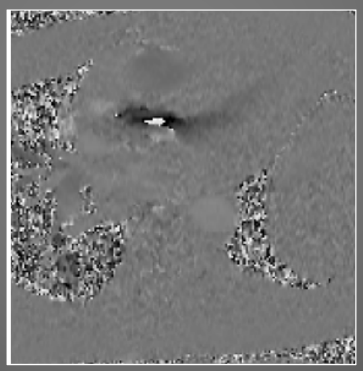
With or without contrast medium

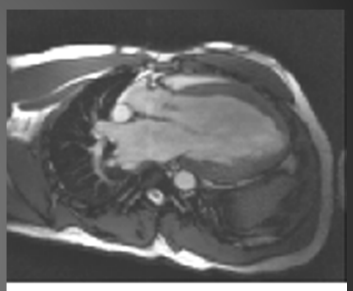
T1 value and extracellular volume: correlate with myocardial fibrosis

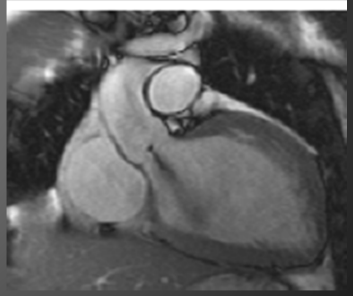


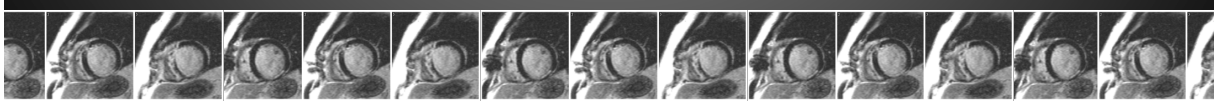
Valvular disease: thickening, stenosis and regurgitation

- Cine and Phase contrast sequences





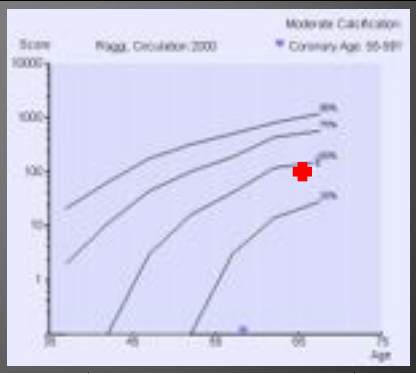




Coronary CT

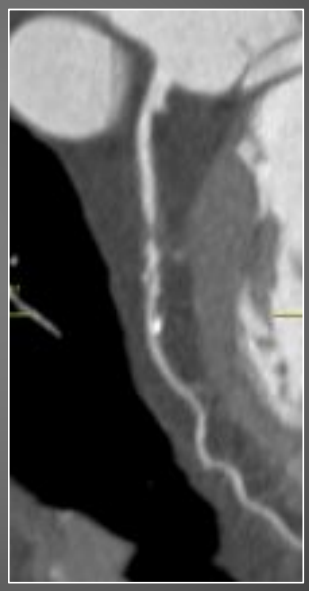
- Calcium scoring: Agatstone score

Artery	Lesions	Volume [mm³]	Equiv. Mass [mg]	Score
LM	0	0,0	0,00	0,0
LAD	2	89,8	10,80	105,6
CX	0	0,0	0,00	0,0
RCA	1	1,9	0,29	0,0
TOTAL	3	91,7	11,09	186,4

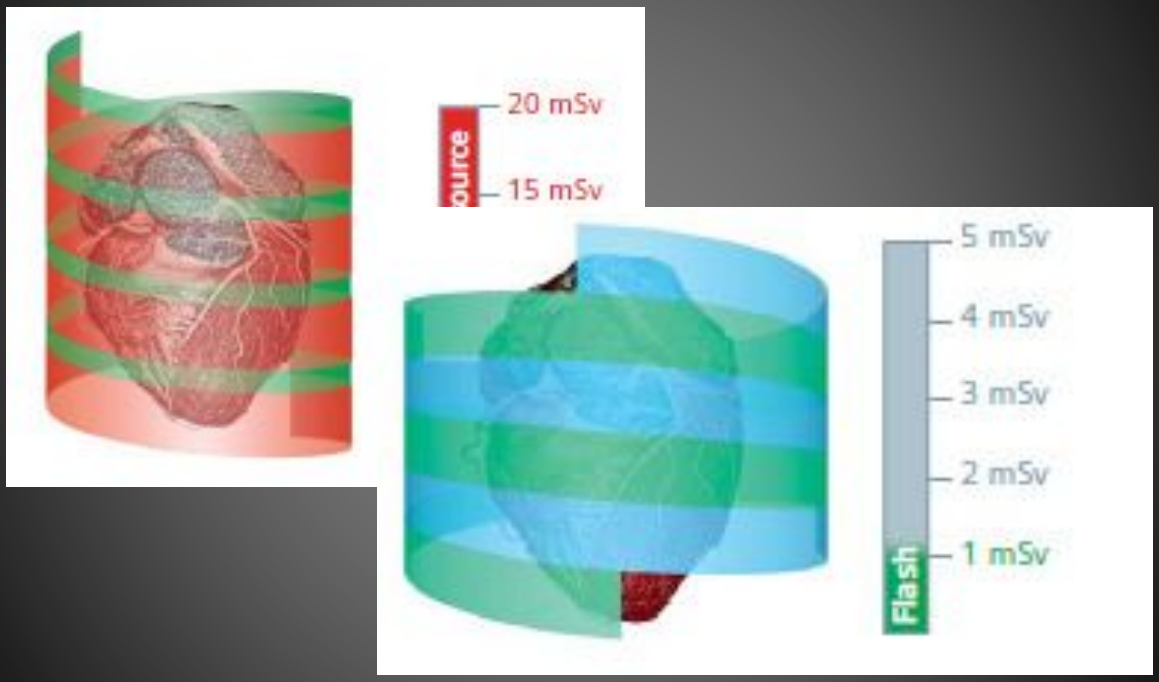


Coronary CT

- Detection of asintomatic CAD



CCT Dose



Conclusions

- The use of non-invasive, non–radiation-based techniques such as echocardiography and cardiac MRI provide an opportunity for regular assessment of the heart for the myocardial, valvular, and pericardial complications of thoracic irradiation.
- CCT for detection of CAD is a potential focus for further research.