CARDIOTOSSICITA' ED ARITMIE

Il parere del radioterapista

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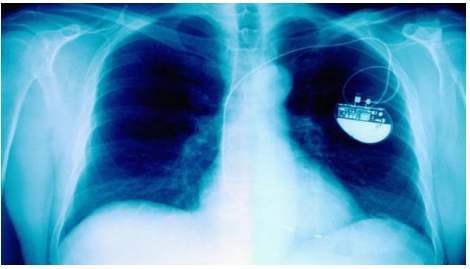
…30 years after….
Lung adenocarcinoma --- left upper lobe---
2.5 cm, no mediastinal pathologic lymphnodes
cT1N0M0
Surgery contraindicated

Radiotherapy and Cardiac Implantable Electronic Device

Registro Italiano Pacemaker e Defibrillatori

Bollettino Periodico 2015



- 24.285 PM
- 15.363 ICD

I NUMERI DEL CANCRO IN ITALIA 2015

- 363.000 new diagnoses
- Radiotherapy in ≈ 50% of patients

- The proper functioning of PM and ICD can be affected by radiation treatment due to the direct or diffuse effects of ionizing radiation and/or electromagnetic interferences produced by linear accelerators on cardiac devices
- After radiation therapy, device failure occurs in about 2.5 % of patients with PM and 6.8 % of patients with ICD *[Zaremba et al, PACE 2015]*
- There is still a significant lack of knowledge regarding the safe management of cancer patients with implantable cardiac devices facing radiation treatment
- Before 2012 the most cited guidelines were AAPM (originating in 1994!!)

Radiation source	a) No use of betatrons
	b) Due to lack of data for other sources, recommendations are given only for betatrons, linear accelerators, and telecobalt sources. Other radiation sources/qualities should only be used after individual risk assessment
Execution of radiation treatment	a) PMs should not be located directly in the beam
	b) The expected dose at the PM should be estimated before first treatment
	c) PM dose >2 Gy: PM interrogation before initiation of RT, once weekly. PM dose 2–10 Gy: early parameter changes might be indicative for imminent PM failure
Patient monitoring	a) Mandatory monitoring of the patient during first RT treatment

Heart Rhythm New Zealand Council (2015)
Radiotherapy position statement

The Cardiac Society of Australia and New Zealand

La Radioterapia dei Tumori della Mammella

Indicazioni e Criteri Guida

Associazione Italiana
di Radioterapia Oncologica
Gruppo di lavoro AIRO per la Patologia Mammaria

REVIEW Open Access

Management of radiation oncology patients with a pacemaker or ICD: A new comprehensive practical guideline in The Netherlands

Coen W Hurkmans[1,8*], Joost L Knegjens[2,8], Bing S Oei[3,8], Ad JJ Maas[4,9,10], GJ Uiterwaal[5,9], Arnoud J van der Borden[6,10], M

DEGRO/DGK guideline for radiotherapy in patients with cardiac implantable electronic devices

Benjamin Gauter-Fleckenstein · Carsten W. Israel · Marc Dorenkamp · Jürgen Dunst · Mattias Roser · Rainer Schimpf · Volker Steil · Jörg Schäfer · Ulrike Höller · Frederik Wenz

CARDIONCOLOGIA 2017
Domande, Risposte E...Dubbi

DEPARTMENT OF ONCOLOGY
UNIVERSITY OF TURIN

Radiotherapy and CIED

Radiation therapy is shifting from use of primarily conventional techniques and conventional fractionations to IMRT and arc techniques and the use of more hypofractionated schedules
The higher fraction dose might lead to a potentially higher dose per fraction to a CIED...

However, the use of more modern techniques has led to a reduced use of high energy photon beams, potentially leading to less dose to a CIED…

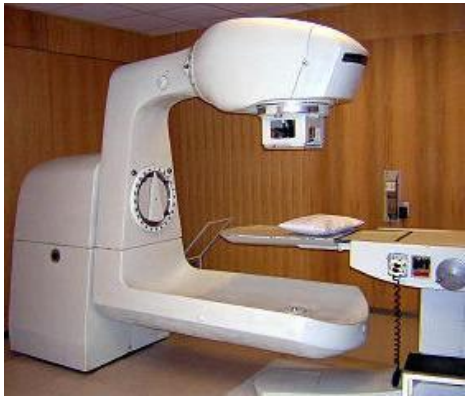
Effects of ionizing radiation and electromagnetic fields on PM and ICD

- In vitro and in vivo clinical studies have shown that ionizing radiation and electromagnetic fields can cause permanent and/or latent damages to CIED due to ionization of semiconductors present in the circuits of these devices, to changes in voltage and to creation of aberrant electrical pathways induced by irradiation itself

- ICD are probably more sensitive to irradiation (5–10 times more than PM) because of their higher sensitivity to diffuse irradiation: a direct exposure to cumulative doses higher than 0,5 Gy can lead to the rupture of the ICD

Effects of ionizing radiation and electromagnetic fields on PM and ICD

- Electromagnetic interference (EMI) may lead to inappropriate sensing of a myocardial potential, resulting inhinibition of the output, fixed rate pacing or reprogramming. These effects are mainly temporary or reversible



- Electromagnetic fields around modern linear accelerators have decreased, reducing the concern to patients with a CIED: EMI dose not seem to be of clinical relevance

Type of device failure during radiotherapy

	Potential error	PM	ICD
Ionizing radiation	Altered stimulation (amplitude, frequency)	x	x
	Altered sensing (over/under sensing)	x	x
	Inhibition of stimulation (pause, asystole)	x	x
	Change in operational mode (incl. asynchronous stimulation)	x	x
	Battery depletion	x	x
	Altered electrode sensing	x	x
	Inhibition of anti-tachyarrhythmia therapy		x
	Altered shock energy		x
	Inadequate shock therapy		x
	Loss of telemetry	x	x
	Loss of function	x	x
Electromagnetic interference	Altered sensing (over/under sensing)	x	x
	Inhibition of stimulation (pause, asystole)	x	x
	Asynchronous stimulation	x	x
	Inhibition of antitachyarrhythmia therapy		x
	Inadequate shock therapy		x
	Reset/reprogramming of device	x	x

Modified from DEGRO/DGK guideline, 2015

In Vitro Studies

Author	Year	CIEDs	Type	Effects
Souliman [56]	1994	18 (15 × 1-chamber and 3 × 2-chamber system), various manufacturers	PM	Irreversible malfunction of all 2-chamber systems between 16.8 and 64.4 Gy; irreversible malfunction of eight 1-chamber systems between 25.2 and70 Gy
Wilm [66]	1994	20 (3 manufacturers)	PM	10 Gy: decrease of stimulatory amplitude; 40 Gy: first loss of function; 90–300 Gy: 19× loss of function (loss of entire stimulation capability)
Röthig [50]	1995	3 manufacturers (no information reg. number of devices)	PM	Failure of all tested systems at 40–90 Gy
Mouton [43]	2002	96 (different models and manufacturers)	PM	Decrease in stimulatory amplitude >10 % (n=63) between 2–130 Gy; intermittent loss of stimulation >10 s (n=39) between 0.15 and 90 Gy; irreversible loss of stimulation (n=48) between 0.5 and 170 Gy
Hurkmans [21]	2005	19 (4 manufacturers)	PM	Irreversible failure of 14 systems between 20 and 130 Gy (loss of stimulation, battery depletion, loss of telemetry); first significant sign of malfunction (telemetry) at 10 Gy
Hurkmans [20]	2005	11 (4 manufacturers)	ICD	Irreversible failure of all systems between 1.5 and 120 Gy (shock delivery not possible, loss of stimulation, loss of sensing); first significant sign of malfunction (decrease in shock energy) at 0.5 Gy
Uiterwaal [62]	2006	11 (4 manufacturers)	ICD	Interference in all ICDs when directly irradiated (starting from 0.5 Gy); misinterpretation as ventricular fibrillation
Kapa [24]	2008	20 (3 manufacturers), incl. 8 CRT systems	ICD	No malfunction due to scatter radiation (4 Gy, 6 MV)
Hashii [14]	2012	10 ICDs (1 manufacturer, 2 models)	ICD	8 ICDs arranged around a water phantom; 2 ICDs in 140 cm distance: software failures in both locations, 8× more often with 18 MV compared with 10 MV; 14–20× more secondary neutrons with 18 MV compared with 10 MV; no difference in scatter radiation (18.8 mSv/10 MV vs. 20.23 mSv/18 MV)
Hashimoto [15]	2012	4 ICDs (1 manufacturer)	ICD	107 GyE proton radiation: only scatter radiation but still exposure to high rate of secondary neutrons; one ICD malfunction every 15 GyE (reset, reversible loss of function); no irreversible failures
Zaremba [67]	2014	10 PM (new), 2 ICD (explanted; 5 manufacturers)	PM/ ICD	Increasing fractional doses up to 150 Gy; all CIEDS were placed in a phantom in the beam; 6/18 MV photons: 14 malfunction in 5 PM with 18 MV; one malfunction in PM with 6 MV (HR 9.11 [95 % (CI): 1.04–79.69]; no failures in ICDs

Table 1. Results for all 11 ICDs

Device	Manufacturer	Model	Malfunction (not point of failure)	Dose at first malfunction (Gy)	Point of failure	Dose at point of failure (Gy)
1	Guidant	Ventak PR1ZH VR HE 1852	Too-low shock energy of 22J	120	No shock	120
2	Guidant	Ventak PR1ZH VR HE 1852		—	No shock	80
3	St. Jude Medical	Photon uDR model V-232	Sensing threshold 65% too low (Vmin)	90	No output	90
4	Medtronic	Marquis dr model 7274 VVE DDDR	Atrial sensing threshold 100% too high	10	Atrial sensing defect	120
			Battery charge time increase by 50%	120		
5	Medtronic	Marquis dr model 7274 VVE DDDR	Battery charge time increase by 40%	120	Complete sensing defect	120
6	Biotronik	Tupos LV/A+	Too-low shock energy of 18J	0.5	No shock and no output	1.5
7	Biotronik	Tupos LV/A+	Too-low shock energy of 21J	0.5	No shock and no output	2.5
8	Biotronik	Tupos LV/A+			No shock and no output	1.5
9	Biotronik	Tupos LV/A+	Too-low shock energy of 21J	10	No output and atrial sensing defect	120
			Sensing threshold 50% too low (Vmin)	20		
10	Biotronik	Tupos LV/A+		—	No shock and no output	0.5
11	St. Jude Medical	Photon uDR model V-232	Sensing threshold 65% too low (Vmin)	90	No output	90

Hurkmans C et al, 2005

Clinical Studies

Author	Year	*n*	Tumor entity or site	CIED	RT dose	Dose CIED/energy	Effects
Kapa [24]	2008	8	Head and neck, lung, breast cancer	PM	30–70 Gy	n.m. (only scatter)/n.m.	No malfunction
Oshiro [48]	2008	8	Thorax, abdomen	PM	36.3–77 GyE protons	0 GyE to CIED/0–69 Gy leads	Reset into fallback mode ($n=1$), deviation from programmed stimulatory frequency ($n=1$)
Gelblum [12]	2009	33	Head and neck, thorax, abdomen, pelvis, legs	ICD	6–86.4/1.8–2 Gy	0.01–2.9 Gy/15 MV	Reset into fallback mode ($n=2$, no ICD in beam)
Ferrara [9]	2010	37	Head and neck, thorax, abdomen, pelvis	PM	8–79.2 Gy	<2 Gy ($n=32$), >2 Gy ($n=5$)	No malfunction
Wadasa-dawala [64]	2011	8	Head and neck, lung, breast cancer	PM	45–70/1.8–2 Gy	0.14–60 Gy (PM partially in beam)/6–15 MV	No malfunction
Soejima [54]	2011	60	Head and neck, thorax, pelvis, breast cancer	PM	20–74 Gy	<2 Gy ($n=59$), >2 Gy ($n=1$)/15 MV	Reset into fallback mode ($n=1$), prostate cancer case
Menard [41]	2011	5	Breast cancer	ICD	32.5–66/2 Gy	<0.1–0.3 Gy/4–6 MV	No malfunction
Croshaw [5]	2011	8	Breast cancer	ICD	34/3.4 Gy HDR-BT/ 38.5/3.85 Gy EBRT	0.99–1.68 Gy/n.m.	No malfunction neither HDR-BT nor EBRT
Makkar [36]	2012	69	Head and neck, breast cancer, lung, abdomen, pelvis, limbs	ICD	BC 45/1.8, rectal cancer 50.4/1.8 Gy	4+123 cGy/16 MV	Reset into fallback mode ($n=2$, lung cancer/ rectal cancer)
Elders [8]	2012	15	Head and neck, lung, abdomen, pelvis, legs	ICD	16–70/2–8Gy	n.m./6–18 MV	Reset into fallback mode, invalid data retrieval, inappropriate tachycardia sensing ($n=5$)

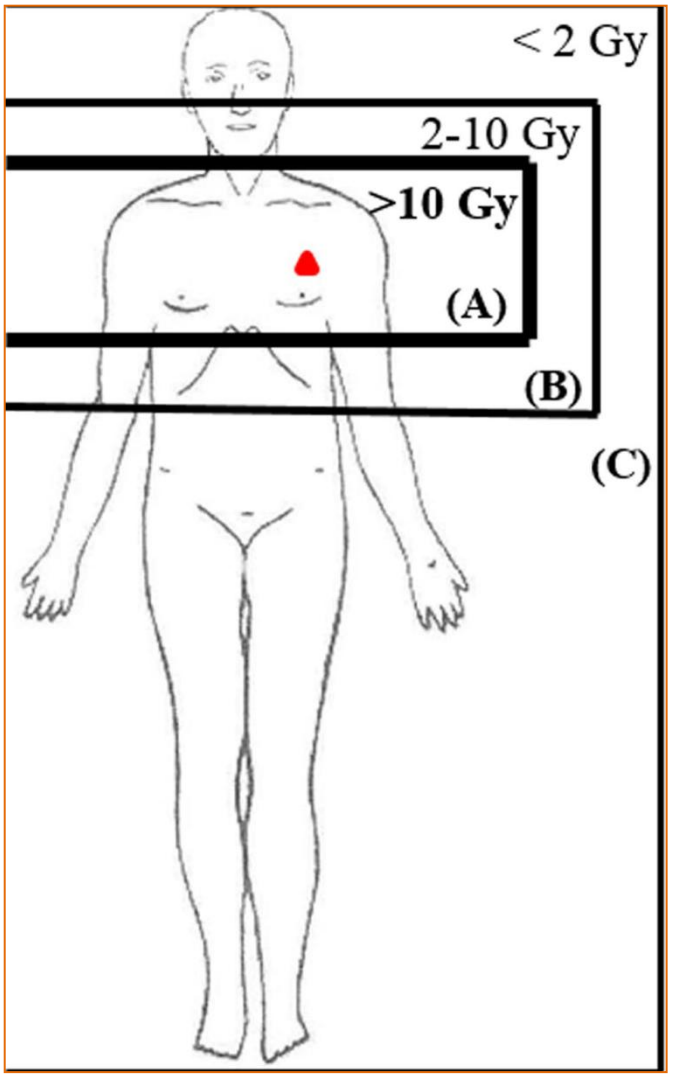
Clinical consequences of CIED malfunction

Malfunctions can lead to different clinical consequences for patients, ranging from symptomatic bradycardia, hypotensive crisis, cardiogenic shock and angina pectoris, to more critical and extreme conditions as asystole, ventricular fibrillation, stroke and death

1) PACING FUNCTION: a complete loss of pacing ability will have major implications for pacing dependent patients
2) TACHY-ARRHYTMIA ICD THERAPY: the probability of ICD therapy occuring at least once during a 6 week course of radiation treatment is about 0.7%, but it's shown in vitro that an ICD could interpret RT induced signals as an arrhytmia, which may leads to inappropriate shock delivery. Such ICD shocks in patients are uncomfortable, although not lethal

RELOCATION MAY BE CONSIDERED!!!!!

How high is the risk for the patient?



- "Pacing dependent" patient

→ the absence of a cardiac intrinsic rhythm of 30 beats per minute for which the abrupt cessation of cardiac pacing due to the abnormal operation of the implanted device creates a situation of extreme emergency

- "Pacing independent " patient

→ intrinsic ventricular rate greater than 30 beats per minute and who have never experienced a situation of clinical emergency related to bradycardia

Potential clinical risk

Table 2 Patient risk categories: cumulative dose to the CIED and pacing independent versus pacing dependent

	< 2 Gy	2-10 Gy	> 10 Gy
pacing-independent	Low risk	Medium risk	High risk
pacing dependent	Medium risk	Medium risk	High risk

Risk defined from the patients' perspective; how high is the risk for the patient? The patient's risk is not equal to the risk of a CIED defect.

Table 7 Differentiation into low-, intermediate-, and high-risk groups: risk for clinically relevant interaction in ICD patients in relation to likelihood of ventricular tachyarrhythmias and accumulated radiation dose to the CIED (parts or whole system)

	<2 Gy	2–10 Gy	>10 Gy
ICD without VT/VFib	Low	Middle	High
ICD with VT/VFib before/after Implantation	Middle	High	High

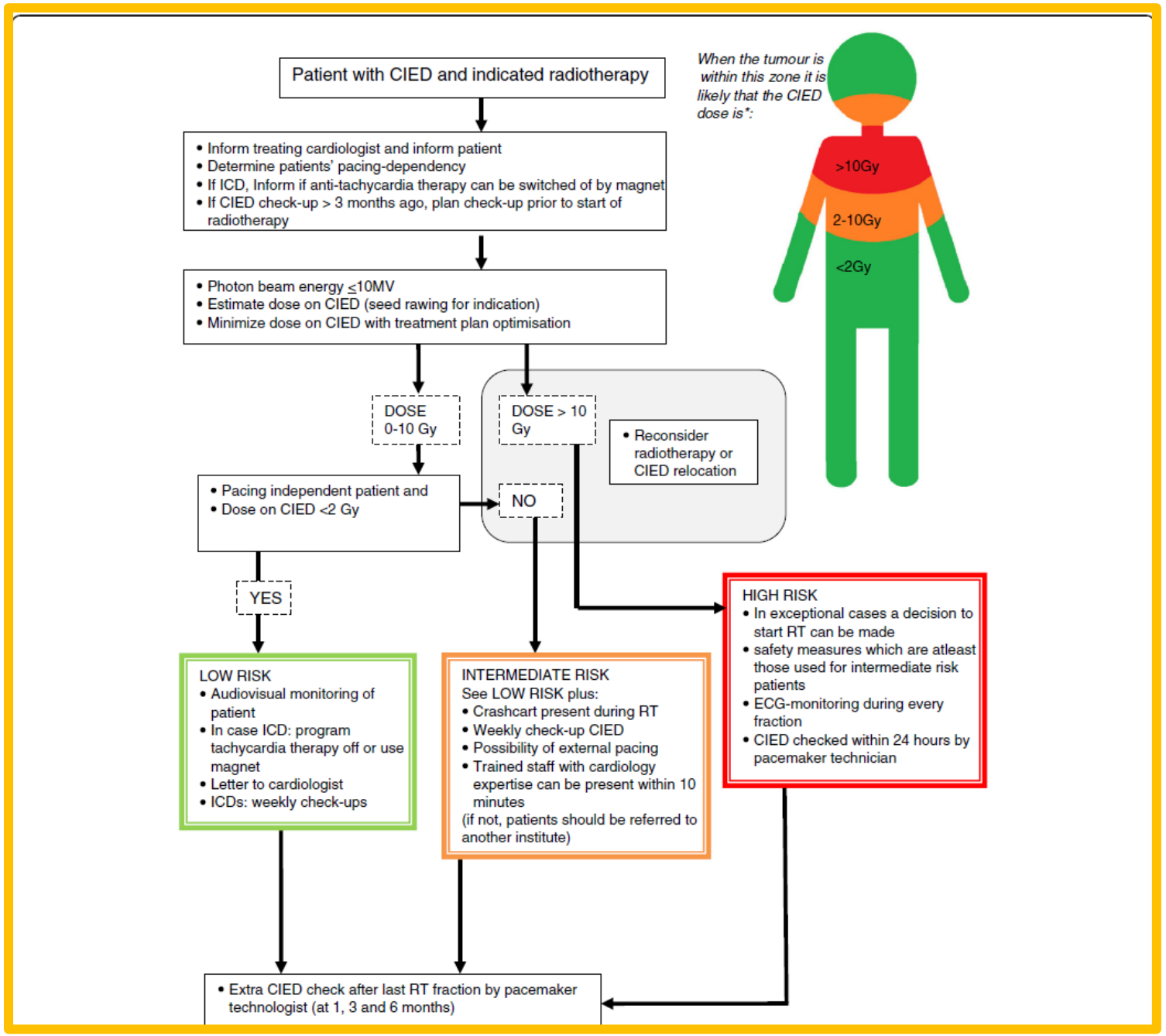
Hurkmans C et al, 2012 DEGRO/DGK guideline, 2015

Patient management

Table 3 Staff and departmental requirements

	Low risk	Medium risk	High risk
Department	- resuscitation protocol	- see low risk+	- see medium risk+
	- good consultancy agreement with cardiology / electrophysiology dept.	- Crash cart including ECG monitor and defibrillator (or AED) available at treatment unit	- ECG monitoring at every fraction
		-external pacemaker available	
Staff	- Radiation oncologist and clinical	- see low risk+	- see medium risk+
	physicist available with sufficient	- cardiologist/pacemaker	
	knowledge in the management of patients with a CIED.	technician should be available within 10 minutes	- trained staff examines ECG
	- Radiation therapy technologists should receive training so they can manage complications experienced by the CIED patient having radiation treatment	if needed - pacemaker technologist to check CIED weekly	- pacemaker technologist checks CIED after every fraction

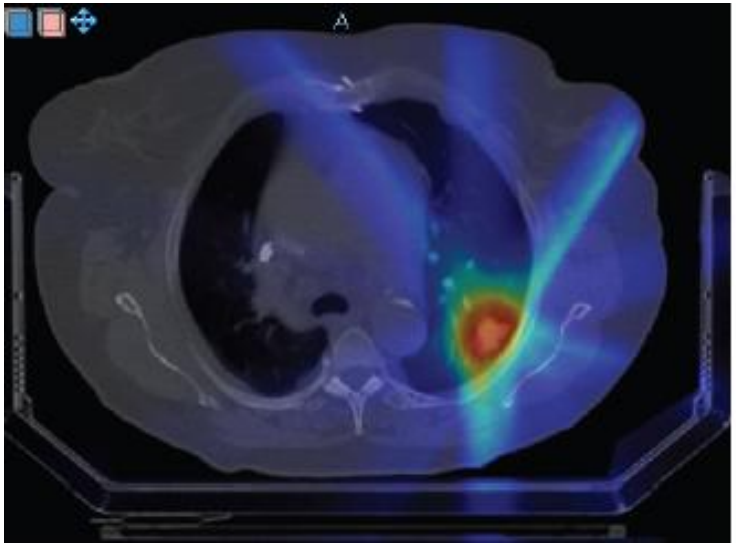
Hurkmans C et al, 2012

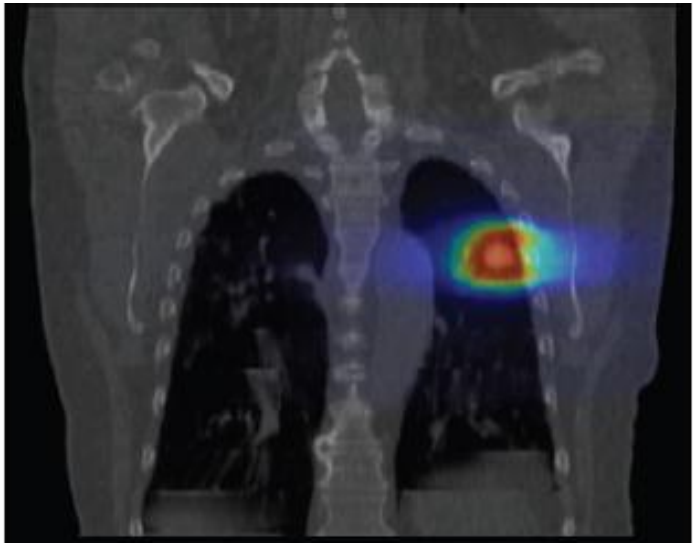

Patient with CIED and indicated radiotherapy
• Inform treating cardiologist and inform patient
• Determine patients' pacing-dependency
• If ICD, Inform if anti-tachycardia therapy can be switched of by magnet
• If CIED check-up > 3 months ago, plan check-up prior to start of radiotherapy
• Photon beam energy ≤10MV
• Estimate dose on CIED (seed rawing for indication)
• Minimize dose on CIED with treatment plan optimisation
DOSE 0-10 Gy
DOSE > 10 Gy
• Reconsider radiotherapy or CIED relocation
• Pacing independent patient and
• Dose on CIED <2 Gy
NO
YES
LOW RISK
• Audiovisual monitoring of patient
• In case ICD: program tachycardia therapy off or use magnet
• Letter to cardiologist
• ICDs: weekly check-ups
INTERMEDIATE RISK
See LOW RISK plus:
• Crashcart present during RT
• Weekly check-up CIED
• Possibility of external pacing
• Trained staff with cardiology expertise can be present within 10 minutes
(if not, patients should be referred to another institute)
HIGH RISK
• In exceptional cases a decision to start RT can be made
• safety measures which are atleast those used for intermediate risk patients
• ECG-monitoring during every fraction
• CIED checked within 24 hours by pacemaker technician
• Extra CIED check after last RT fraction by pacemaker technologist (at 1, 3 and 6 months)
When the tumour is within this zone it is likely that the CIED dose is*:
>10Gy
2-10Gy
<2Gy

P. L. female 75 y.o.

January 2011: nodular lesion at the apex of the left lung;
PET SUV max 4.6→ clinical proof of malignancy

Cardiovascular history
1009: acute miocardial infarction (CABG + left ventricular aneurismectomy)
2004: cronic heart disfunctiion → ICD + biventricular PM
2009: last episode of VT, correctely treated by ICD
Ex smoker- cronic kidney disease – HTA NIDDM

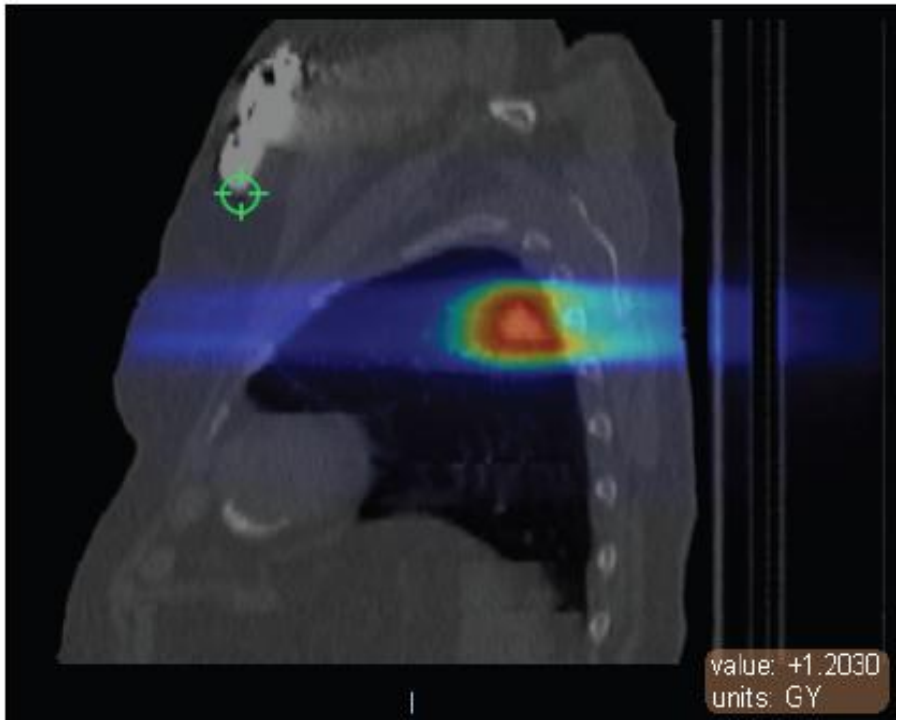




March 2011

- Stereotactic Ablative Radiotherapy→ 54 Gy in 3 fractions
- Switch off tachycardia-therapy before every fraction
- Crashcart present during RT
- ICD check and reprogramming after every fraction

Structure	Volume (cm³)	Plan Name	Min Dose Gy	Max Dose Gy	Mean Dose Gy
AORTA ASCENDE	63.344	1guscio	0.646	8.409	1.778
AORTA DISCEND	114.232	1guscio	0.000	15.291	2.117
COSTA	6.384	1guscio	13.286	41.708	27.002
CUORE	1242.776	1guscio	0.013	6.114	0.865
ESOFAGO	55.232	1guscio	0.000	5.704	1.534
External(Unsp.Tiss	22929.048	1guscio	0.000	50.189	1.207
ICD	99.640	1guscio	0.000	1.686	0.228
ITV	7.400	1guscio	46.054	52.595	49.753
PTV	18.416	1guscio	35.690	52.595	48.268
Polm dx	1519.496	1guscio	0.000	10.232	0.665
Polm sn	1461.240	1guscio	0.000	52.595	6.272
guscio	6381.736	1guscio	0.000	18.537	0.771



Follow up

February 2017

- NED

- RTOG chronic radiological toxicity G1, no clinical toxicity

  - December 2011→ major ventricular arrhytmia, correctly recognised and cardioverted by ICD

Clinical experience @ University of Turin

19 patients (14 males, 5 females)

2007-2016

Median age: 76.5 yo
NSCLC; hypofractionated RT
→ most of patients SABR
→ Dmax CIED: 0.5 Gy

Median ventricular threshold:
0.91 ± 1.01 pre-RT
1.03 ± 1.06 post-RT P= 0.07

Median atrial threshold:
0.86 ± 0.89 pre
0.97 ± 0.92 post P= 0.12

Battery life pre - RT→ 77 months
Battery life post- RT→68.5 months
P: 0.06

Take home messages….

- ✓ A close collaboration between cardiologist, radiation oncologist and physicist is mandatory

- ✓ Use of energy equal or below 6 MV is preferable
- ✓ Total dose $\leq$ 2 Gy to the PM
  $\leq$ 1 Gy for the ICD
- ✓ Weekly device check during the full period of radiation therapy in low- and intermediate-risk patients with an ICD and in intermediate-risk patients with a PM
- ✓ Expert device evaluation (PM or ICD) within 24 h after the end of each session of radiotherapy in high-risk patients
- ✓ Equipment for cardiopulmonary resuscitation available during the treatment period

Grazie per l'attenzione!!!!!