

ORIGINAL ARTICLE

Radiation therapy planning of a breast cancer patient with in situ pacemaker—challenges and lessons

ANUSHEEL MUNSHI¹, TABASSUM WADASADAWALA¹, PRAMOD KUMAR SHARMA², DAYANANDA SHARMA², ASHWINI BUDRUKKAR¹, RAKESH JALALI¹ & KETAYUN A. DINSHAW¹

¹Department of Radiation Oncology and ²Department of Radiation Physics, Tata Memorial Hospital, Mumbai, India

Abstract

A postmenopausal lady with an in situ pacemaker developed a lump in the left breast and was diagnosed to have breast cancer. The patient underwent breast conservative surgery and was planned for post operative radiotherapy. The location of the tumor relative to the pacemaker provided a unique challenge in planning radiotherapy and the patient had an uneventful post radiotherapy course. A literature review revealed that modern generation pacemakers are very sensitive to radiation compared to their older counterparts. The present article makes suggestions towards reducing dose in radiotherapy planning in pacemaker patients.

With more than one million new cases each year, female breast cancer is the second most common cancer in the world and the most common cancer among women [1]. Breast conserving therapy (BCT) is increasingly being integrated into the management of breast cancer. The obvious advantages of BCT are an equivalent disease free and overall survival rate as compared to mastectomy with preservation of the breast [2,3]. Over the past decades, there has been an increase in the average life expectancy rate throughout the world, albeit with comorbidities such as diabetes, hypertension and strokes [4]. One of the common conditions in elderly age group includes conduction defects in the heart secondary to ischemic heart disease [5]. Often this necessitates the placement of a pacemaker to regulate the electrical activity of the heart. A postmenopausal lady with an in situ pacemaker developed left sided breast cancer. The patient underwent breast conservative surgery (BCS) and was planned for post operative radiotherapy. The location of the tumor relative to her pacemaker provided a unique challenge in planning radiotherapy. In this article we are discussing the issues in radiotherapy planning of this patient with an in situ pacemaker and presenting a review of the current literature.

Case report

A 64-year-old postmenopausal multiparous lady, known diabetic and hypertensive, was investigated for repeated episodes of giddiness and hypertension refractory to antihypertensives. She was detected to have a 2:1 heart block with right bundle branch block and left anterior hemi block. She subsequently underwent permanent pacemaker placement (St Jude Pacemaker; Affinity Model DR 5330). Three years later, she presented with history of lump in the left breast of 3 months duration. On clinical examination there was a 2.5 × 2.5 cm hard lump in upper outer quadrant of the left breast. FNAC was positive for ductal carcinoma. Echocardiography before surgery was suggestive of concentric left ventricular hypertrophy (LVH) with diastolic dysfunction and a left ventricular ejection fraction (LVEF) of 50%. Electrocardiogram (ECG) showed a normal pacemaker rhythm. She underwent BCS under close cardiac monitoring by a cardiologist and a pacemaker engineer. The histopathology revealed infiltrating ductal carcinoma grade II with a pathologic tumor size of 2.5 × 2.5 × 2.0 cm. All the cut margins were free. Axillary sampling revealed eight negative nodes. The specimen was ER negative,

PR positive and *cerbB2* negative. Postoperative 2D-echocardiography revealed a LVEF of 50% with no appreciable change as compared to baseline. Cardiology consultation for evaluation of the pacemaker functioning was documented to be normal. In view of her favorable histopathology and her cardiac ailment, adjuvant chemotherapy was not given and she was directly referred for postoperative radiotherapy. For radiotherapy planning, serial CT slices were taken with appropriate immobilization. The acquired images were transferred to the planning system. During planning, it was realized that whole breast radiotherapy would result in direct irradiation of the lower half of the pacemaker due to its location within the radiation portal. Since her clinical and pathological profile fulfilled the current American brachytherapy Society (ABS) and National Surgical Adjuvant Breast and Bowel Project (NSABP) criteria for Accelerated Partial Breast Irradiation (APBI), it was decided to leave the upper portion of the breast unirradiated. Her final target volume consisted of the lumpectomy cavity (located in the central and a uniform 2.5 cm margin (with editing towards the chest wall and skin) [6]. In the subsequent radiotherapy portal, the entire target was covered by the tangentials (Figure 1, central slice) while sparing the pacemaker whose inferior edge remained more than 3 cm away from the upper border of the portal (Figure 2). The dosimetry of the case was done in the Cadplan planning system (Varian). In view of the large size of the breast, 10 MV x-rays were used in treatment planning with a 15 degree bilateral wedge for appropriate dose distribution. Care was taken to see that besides the pacemaker device, the leads going

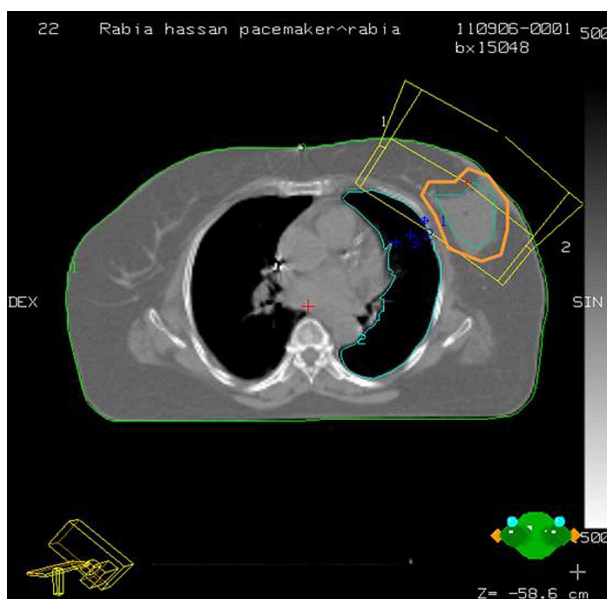


Figure 1. Axial view showing the beam arrangement and the appropriate coverage of lumpectomy site.

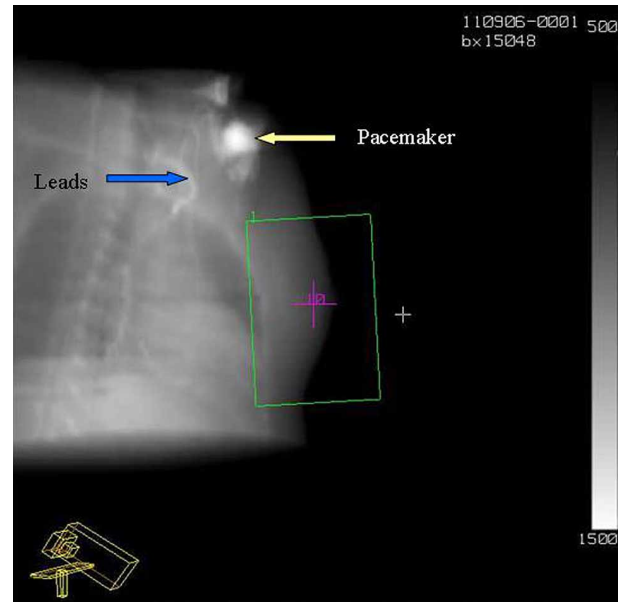


Figure 2. Digital Reconstructed Radiograph (DRR) showing the pacemaker and the leads in relation to the radiation beam.

to the heart were also kept out of the radiotherapy portal. For the first and subsequent few fractions during the course of radiotherapy, continuous ECG monitoring was done during the radiotherapy beam on time. A back-up temporary pacemaker was kept ready for use in case permanent pacemaker malfunction occurred during radiotherapy. The gross ECG pattern before and during radiotherapy did not reveal any change. The parameters of the pacemaker were recorded pre radiotherapy and during the time the radiotherapy beam was on (Table I). Dosimetry with diodes was done on the first day to measure dose at the inferior most edge of the pacemaker (closest part of pacemaker to the upper border of the field (Table II). No event of bradycardia/tachycardia/arrhythmia was recorded. The pacemaker engineer evaluated the pacemaker parameters every week. ECG was done before, during and after completion of course of radiotherapy. By our estimate, the pacemaker received a dose of $15.37 \text{ cGy} \times 28 \text{ fractions} = 4.3 \text{ Gy}$ (Table II). The varying depth of the pacemaker from the surface was recorded (Table III). Since our recording was on the surface

Table I. Pacemaker functioning before and during radiotherapy.

Parameter	Pre radiotherapy	During radiotherapy
Atrial capture threshold	0.5 V	0.5 V
Ventricular capture threshold	0.5 V	0.5 V
Lead impedance atrial	732 ohms	697 ohms
Lead impedance ventricular	622 ohms	631 ohms
Ventricular Pulse current	4 mA	5.6 mA
Atrial pulse current	3.3 mA	5.1 mA

Table II. Dosimetry recording of diode.

	Entrance dose recorded
Total prescribed isocenter dose	180 cGy per fraction
Medial tangential	9.51 cGy per fraction
Lateral tangential	5.86 cGy per fraction
Total diode dose recorded	15.37 cGy

Entrance dose from 180cGy at isocentre.

Gap between field edge and the inferior edge of pacemaker = 3 cm.

and in view of our dosimetric findings, we decided to limit the total dose of radiotherapy to 50.4 Gy only at 1.8 Gy per fraction. Also, we did not give boost field with electrons in view of the increased risk of dose scatter with electrons. At 10 months of follow-up, the patient is disease free and the pacemaker is functioning normally.

Discussion

The device

The pacemaker consists of a main device encased in a seal whose electrodes or leads are threaded through intravenously into the cardiac chamber where it lies in contact with the cardiac musculature. It is made of computer chips and a small but long life (5 to 10 years) battery in a sealed case. It can be single chamber (right ventricle), dual chamber (right atrium and right ventricle) or three chamber (right atrium and both ventricles) pacemaker. It is usually placed in a subcutaneous pocket over the pectoral muscles in the left infraclavicular region, posing a problem for delivering radiotherapy for lymphomas, breast, lung, head and neck, thyroid and esophageal cancers. It may also possess sophisticated programmable software and facilities for recording events.

Certain types of electric and magnetic energy can interfere with the operation of the pacemaker, a phenomenon known as electromagnetic interference (EMI) [7–11]. The devices causing EMI are of two

Table III. Depth of pacemaker from skin surface at different axial levels (in cm).

	S	M	D
Axial CT scan Level (at 1 cm each)			
–44.1	1.57	2.25	2.99
–45.1	1.82	2.76	3.82
–46.1	2.27	2.99	4.02
–47.1	2.63	2.89	3.48
–48.1	2.78	3.40	4.06

S = Superficial aspect of pacemaker (facing skin).

M = Mid point of pacemaker.

D = Deepest aspect of pacemaker.

Table IV. Sources of electro magnetic interference (EMI) with pacemaker.

Medical	Non-medical
Radiotherapy	Poorly grounded electric appliances
Transcutaneous electrical nerve stimulation	Industrial generators
Magnetic Resonance Imaging, PET	Metal detectors security checks at airports & stores (electronic article surveillance EAS)
Lithotripsy, dental scaler, RFA	Magnets
Arc welders	Radiotransmitters/ Radioemitters
Electrocautery, ECT	Electric shavers/drills
Diathermy, Acupuncture	Large heaters

types: 1) Conducting: involving a direct contact of the EM source with body. Examples of this include electrocautery or defibrillators. 2) Radiating: requiring no physical contact. Examples include MRI, PET, lithotripsy and megavoltage radiotherapy delivery (Tables IV and V) [10,11].

The mechanism of damage of a pacemaker during radiotherapy includes: a) Ionization of semiconductor material; b) EMI from linear accelerators; c) Abnormal current flows; d) Changes in threshold voltage [10]. The manifestation of damage includes dropped beats, pacemaker induced tachycardia, runaway rhythm, circuitry failure, pacemaker malfunction (erratic pacing, sensing anomalies) and sudden death. [8,11–14].

Threshold doses

Older generation pacemaker devices based on bipolar semiconductor were very radioresistant. These tolerated doses from 100 to 460 Gy, well above the therapeutic radiotherapy dose for any cancer [7,8]. Hence these devices did not pose any hindrance in radiotherapy delivery. Modern generation programmable pacemakers containing the complementary metal-oxide semiconductors (CMOS) are very radiosensitive to megavoltage radiation and are affected by doses as low as 0.15 Gy. Therefore these devices pose therapeutic dilemmas in delivering

Table V. Safe procedures with pacemaker in situ.

Medical	Non-medical
Computerized Tomography	Microwave ovens, blenders, toaster
USG	Cellular phones
Mammography	TV, VCR
X-rays	Electric blankets, knives, stoves
Fluoroscopy	Garage door openers

the standard treatment [9,10]. Each new model in the market differs from older models in some way, either in design or structure or software program, thereby greatly influencing the radiosensitivity and making comparison difficult.

At present there are no uniform recommendations from the manufacturers and the available recommendations are unreliable. Most of the literature addressing this issue is in the form of single patient case reports or in vitro studies only (Table VII) [15–20,22,23]. The only available recommendations are from the AAPM published in 1994, of which there is no recent official updated report. They recommended that maximum dose to the pacemaker be limited below 2 Gy [24]. However, no recommendation for the effect of dose rate has been made. Until sound recommendations become available, it is the responsibility of the individual radiotherapy departments to identify and develop formal protocols for cancer patients with pacemakers especially in the planning and delivery of radiotherapy. Also the safety of high dose rate brachytherapy in case of implanted pacemaker close to target volume and of electronic portal imaging devices is not known. The St Jude's pacemaker guidelines published in June 1998 state that radiation damage to CMOS circuitry can occur at 2000 rads and that the present SJ pacemakers are tested up to 30 Gy. They recommend a lead apron over the generator as it is always to be kept out of field [25]. Medtronic guidelines recommend a total allowable dose to the pacemaker up to 5 Gy and they also require generator to be moved outside the field [26]. Guidant guidelines have recommended that there is "no safe dose" which can be recommended as total allowable dose [27].

Possible solutions and suggestions

For medium and high-risk patients, alternative treatment modalities such as surgery, hormone therapy or chemotherapy should be pursued if they are equally valid treatment options and appropriate for that patient. Table VI gives the risk stratifications

Table VI. Risk categories for treatment of pacemaker patients by radiotherapy.

Category	Criteria
Low risk	Patient not pacemaker dependent, pacemaker not directly in RT field, dose likely to less than 2 Gy. Baseline and subsequently weekly ECG should suffice
Medium risk	Pacemaker dependent, pacemaker not directly in RT field, dose likely to less than 2 Gy.
High risk	Pacemaker dependent, pacemaker not directly in RT field but dose more than 2 Gy or a pacemaker placed directly in RT field.

of a patient with a pacemaker [9]. Medium and high risk categories require personnel trained in advanced life support and on call cardiac team to tackle emergency. High risk cases also require continuous cardiac monitoring during radiotherapy from an outside room.

A baseline ECG should be obtained in all patients with pacemakers. This will help in assessment of pacemaker dependency. However, formal interrogation in a pacemaker clinic may also be required and is probably desirable before commencing radiotherapy.

Simple changes in the treatment plan may reduce the dose to the pacemaker to a low risk level. As literature on interaction of modern radiosensitive pacemakers is limited, only in the form of case-reports, pre-clinical animal or dosimetric studies only, systematic cohort studies to assess the short and long term effect of radiation on the functional integrity of pacemakers are essential. This needs to be accorded a high priority by large cooperative oncology groups since with the inevitable ageing of the population and expanding indications for pacemaker implantation, a considerable proportion of cancer patients will have pacemakers in the future. Surgically shifting the pacemaker to a region of less radiotherapy dose can also be considered.

Radiation planning with pacemaker devices

The low energy, kilovoltage x-rays used in simulation for radiotherapy fluoroscopy simulators and CT scanners are unlikely to cause malfunction of pacemakers and can be safely used for radiotherapy planning [25,28]. The majority of the patients encountered in the radiotherapy department do not have a pacemaker directly in the beam and therefore a radical change to the prescribed treatment is usually not necessary. The issue of radiation and pacemaker is more relevant in tumors related to breast, lung, esophagus and other thoracic tumors. There has been no demonstrable volume effect with the pacemaker for radiotherapy damage. It needs to be noted that there is no safe radiation threshold for megavoltage radiation to preclude their effect on the pacemakers. The cardinal rule is that radiation dose to the pacemaker is the dose to any part of the device (including the leads). Also there does not appear to be any consistent way to predict how a device will fail or at what radiation dose failure will occur. The following possible suggestions are made to keep dose to the pacemaker as low as possible: a) Considering other treatment options (non radiotherapy) if they are equally efficacious; b) Surgically shifting the pacemaker to a region of less radiotherapy dose (e.g. contra lateral side); c) Excluding pacemaker from radiotherapy portal in case it is decided to give

Table VII. Published reports of irradiation in patients with pacemaker.

Author	Year	Reference	Diagnosis	Total dose prescribed	Dose to pacemaker	Beam Type	Observation/Comments
Katzenberg et al.	1982	8	Breast cancer	36 Gy	<36 Gy	–	Pacemaker malfunction (Pacemaker within RT portal)
Quertermous et al.	1983	13	Bronchogenic carcinoma	50.8 Gy	20 Gy	–	Runaway rhythm (Pacemaker within RT portal)
Pourhamidi et al.	1983	14	Esophageal cancer	63 Gy	15 Gy	Gamma rays	Pulse generator damage (Pacemaker close to RT portal)
Lewin et al.	1984	15	Axillary Heman-gio-Pericytoma	19.8 Gy	19.8 Gy	X-rays	Tachycardia (CMOS based pacemaker within RT portal)
Lee et al.	1986	12	Breast cancer	39.6 Gy	<40 Gy	X-rays	Tachycardia (Pacemaker was within RT portal)
Brooks et al.	1988	16	Bronchogenic carcinoma	35 Gy	<35 Gy	X-rays	Tachycardia (Presented as emergency, relieved by magnet application)
Mueller et al.	1990	17	Bronchogenic carcinoma	64 Gy	6.2 Gy	X rays	No effect (Pacemaker was outside RT portal)
Ngu et al.	1993	18	Bronchogenic carcinoma	–	0.5 Gy	Gamma rays	Nil (Pacemaker was outside RT portal)
Raitt et al.	1994	19	Thyroid malignancy	4.8 Gy	0.8 Gy	Neutrons	Runaway rhythm
Nibhanupudy et al.	2001	20	Breast cancer	<60 Gy	<2 Gy	X-rays	Nil (Pacemaker shifted out of RT portal)
Riley et al.	2004	21	Bronchogenic carcinoma	63 Gy	5.6 Gy	X-rays	Nil (Pacemaker was outside RT portal)
Li Diem et al.	2004	22	4 patients with varied tumors	40–70 Gy	–	X-rays/ Gamma rays	Nil
Sepe et al.	2007	23	Laryngeal cancer	60 Gy	2.5 Gy	X-rays	Nil (Pacemaker was outside RT portal)

radiotherapy; d) Wherever possible, to calculate the approximate dose to the pacemaker before initiation of treatment. In vivo dosimetry is preferred but is usually difficult.

Radiotherapy technique should involve judiciously using different beam angles including non-coplanar beam arrangement, radiation quality and modality, asymmetric jaws (towards the pacemaker end to reduce the effect of divergent beam), accessories for beam shaping like multileaf collimators, wedges and metal alloy shielding. Specialized techniques in the form of 3DCRT or IMRT can be employed taking the pacemaker as the organ at risk [21]. It seems prudent to restrict the maximum dose to the pacemaker to less than 2 Gy or at least fulfill the individual manufacturer's specified recommendations. It is advisable to avoid using equipment liable to produce electromagnetic interference

(EMI) like beam gating, electronic portal vision device (EPID) or in room accessories including breathe control systems. Finally, the pacemaker can be shielded with a block or Multi leaf collimator (MLC). The option of interstitial high dose rate brachytherapy can be used in appropriate instances.

Suggestions for manufacturers

The protective measures, which can be incorporated into the pacemaker, include the introduction of an anti-interference circuit and use of bipolar electrodes, titanium casing and asynchronous stimulation [29]. Other measures include incorporation of a band pass filter, which prohibits the entry of signals that are above or below a certain frequency threshold [29]. The manufacturer should also be asked to provide radiation tolerance information regarding

relative sensitivity of the pacemaker to previous models. It has to be noted that not all data would be in the public domain and technological improvements occur all the time. Radiation tolerance data pertaining to a particular model are essential. The make and model of the pacemaker, and the manufacturers' recommendations regarding safe doses for that particular model of pacemaker should be ascertained before radiation planning.

To summarise, modern day pacemakers are much more sensitive to radiation than their primitive counterparts. As such, radiation oncologist especially ones dealing with breast and thoracic tumors need to be aware of the limitations in radiotherapy planning with a pacemaker in situ. Even after careful planning, dosimetry should be performed whenever possible to assess the actual dose being received by the pacemaker so that timely adjustments in total dose and treatment techniques can be made.

References

- [1] Kamangar F, Dores M, Anderson F. Patterns of cancer incidence, mortality, and prevalence across five continents: Defining priorities to reduce cancer disparities in different geographic regions of the world. *J Clin Oncol* 2006;24:2137–50.
- [2] Fisher B, Anderson S, Bryant J, Margolese R, Deutsch M, Fisher E. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002;347:1233–41.
- [3] Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* 2002;347:1227–32.
- [4] Mond H, Irwin M, Morillo C, Ector H. The world survey of cardiac pacing and implantable cardioverter defibrillators: Calendar year 2001. *Pacing Clin Electrophysiol* 2004;27:955–64.
- [5] Bernstein D, Parsonnet V. Survey of cardiac pacing and implanted defibrillator practice patterns in the United States in 1997. *Pacing Clin Electrophysiol* 2001;24:842–55.
- [6] Patel R, Das R. Image guided breast brachytherapy: An alternative to whole breast radiotherapy. *Lancet Oncol* 2006;7:407–15.
- [7] Walz BJ, Reder E, Pastore O, Littman P, Johnson R. Cardiac pacemakers. Does radiation therapy affect performance? *JAMA* 1975;234:72–3.
- [8] Katzenberg A, Marcus I, Heusinkveld S. Pacemaker failure due to radiation therapy. *Pacing Clin Electrophysiol* 1982;5:156–9.
- [9] Sundar S, Symonds P, Deehan C. Radiotherapy to patients with artificial cardiac pacemakers. *Cancer Treat Review* 2005;31:474–86.
- [10] Last A. Radiotherapy in patients with cardiac pacemakers. *Br J Radiol* 1998;71:4–10.
- [11] Neihaus M, Terbenjohanns J. Electrical interference in patients with implanted pacemakers or cardioverter-defibrillators. *Heart* 2001;86:246–8.
- [12] Lee W, Huang K, Mechling E. Runaway atrioventricular sequential pacemaker after radiation therapy. *Am J Med* 1986;81:883–6.
- [13] Quertermous T, Megahy S, Das Gupta S. Pacemaker failure resulting from radiation damage. *Radiology* 1983;148:257–8.
- [14] Pourhamidi H. Radiation effect on implanted pacemakers. *Chest* 1983;84:499–500.
- [15] Lewin A, Serago F, Schwade G, Abitbol A, Margolis S. Radiation induced failures of complementary metal oxide semiconductor containing pacemakers: A potentially lethal complication. *Int J Radiat Oncol Biol Phys* 1984;10:1967–9.
- [16] Brooks C, Mutter M. Pacemaker failure associated with therapeutic radiation. *Am J Emerg Med* 1988;6:591–3.
- [17] Muller-Runkel R, Orsolini G, Kalokhe P. Monitoring the radiation dose to a multiprogrammable pacemaker during radical radiation therapy: A case report. *Pacing Clin Electrophysiol* 1990;13:1466–70.
- [18] Ngu L, O'Mealey P, Johnson N, Collins C. Pacemaker function during irradiation: In vivo and in vitro effect. *Australas Radiol* 1993;37:105–7.
- [19] Raitt H, Stelzer J, Laramore E, Bardy H, Dolack L, Poole E, et al. Runaway pacemaker during high-energy neutron radiation therapy. *Chest* 1994;106:955–7.
- [20] Nibhanupudy R, de Jesus A, Fujita M. Radiation dose monitoring in a breast cancer patient with a pacemaker: A case report. *J Natl Med Assoc* 2001;93:278–81.
- [21] Riley B, Gracia J, Guerrero. The utilization of 3-Dimensional noncoplanar treatment plan to avoid pacemaker complications. *Med Dosim* 2004;29:92–6.
- [22] Li DM, Xu B, Xu XN. Radiotherapy of tumor patients implanted with permanent cardiac pacemaker: 4 cases report. *Ai Zheng* 2004;23:722–3.
- [23] Sepe S, Schaffer P, Krimmel K, Schaffer M. Irradiation treatment of laryngeal cancer in a patient with an implantable cardioverter-defibrillator (ICD). *Onkologie* 2007;30:378–80.
- [24] Marbach R, Sontag R, Van Dyk J. Management of radiation oncology patients with implanted cardiac pacemakers: Report of AAPM Task Group No. 34. American Association of Physicists in Medicine. *Med Phys* 1994;21:85–9.
- [25] St. Jude Medical Technical Services. Radiation Revision 9/02. Sylmar, CA: St. Jude Medical Technical Services; 2000. p 1–3.
- [26] Medtronic USA Inc. Technical services. Radiation and pacemakers. Minneapolis: Medtronic USA Inc.; 2002. p 1–2.
- [27] Guidant Corporation Cardiac Rhythm Management Technical Services. The impact of therapeutic radiation on guidant implantable pacemakers (IPMs) and implantable cardioverter defibrillators (ICDs). Revision L02/13/03, St Paul, MN: Guidant Corporation; 2003. p 1–6.
- [28] Rothig H, Wiedemann D, Herrmann T, Burk G. The functional efficiency of cardiac pacemakers as affected by ionizing radiation. *Radiobiol Radiother* 1990;31:341–50.
- [29] Lewin A, Serago F, Schwade G. Electromagnetic interference in cardiac rhythm management devices. *AACN Clin Issues* 2004;15:391–403.