EXPERT REVIEWS

Renaissance of contact x-ray therapy for treating rectal cancer

Expert Rev. Med. Devices 8(4), 483–492 (2011)

Jean-Pierre Gérard[†1], Arthur Sun Myint[2], Olivier Croce[3], Jacob Lindegaard[4], Anie Jensen[4], Robert Myerson[5], Jean-Michel Hannoun-Lévi[1] and Serge Marcie[1]

[1]*Centre Antoine-Lacassagne, 33 Avenue de Valombrose, 06189 Nice Cedex 2, France*
[2]*Clatterbridge Centre for Oncology, NHS Foundation Trust, Wirral, UK*
[3]*Faculté des Sciences, Université de Nice – Sophia Antipolis, France*
[4]*Department of Oncology, Aarhus University Hospital, Aarhus, Denmark*
[5]*Washington University School of Medicine, St Louis, MO, USA*
[†]*Author for correspondence: jean-pierre.gerard@nice.fnclcc.fr*

Contact x-ray therapy (CXRT) with 50 kV has proven to be an efficient radiation therapy technique to achieve local control and rectal preservation for early rectal adenocarcinoma. Despite these results, CXRT has not been used due to the shortage of the no longer manufactured Philips RT 50™ unit. Recently, a new CXRT machine (Papillon 50™) became available on the market. This machine delivers a beam of 50 kV with a dose rate close to 15 Gy/min and has a percentage depth dose of 50% at 6–7 mm. The applicator size varies from 2–3 cm in diameter. Due to the original design of the main tube, treatment delivery is quick and more comfortable for the patients. An online viewing system incorporated in the tube allows a good visualization of the tumor with improved accuracy of radiation delivery. An international collaborative trial (Contact Endoscopic Microsurgery [CONTEM]) was set up to accrue approximately 300 cases of rectal adenocarcinoma staged T1, T2 or early T3 tumors in the UK, France, Denmark and Sweden. This trial should confirm the role of CXRT in curative treatment with organ preservation for early rectal cancers.

Keywords: conservative treatment • contact radiotherapy • Papillon 50™ • rectal cancer

Past clinical experience with contact x-ray treatment in rectal cancer: reasons for progressive abandonment

Contact x-ray treatment (CXRT) with 50-kV photon was initiated in Germany in the 1930s to provide an alternative to radium brachytherapy for cervix uterine carcinoma. It was first used to treat rectal cancer in the 1950s in Montpellier (France) and was popularized by Papillon in Lyon (France) using the Philips RT 50™ machine. This unit delivered a 50-kV x-ray beam with a source skin distance (SSD) of 4 cm and a dose rate of 20 Gy/min. The rectal applicator was 3 cm in diameter.

Between 1960 and 1990 Papillon treated 310 patients with CXRT alone for selected T1N0 rectal adenocarcinoma and achieved a 90% long-term local control without toxicity and excellent rectal function conservation [1]. These results were duplicated by many centers in France, Europe and North America [2–6]. Since the 1990s staging of rectal cancer, which initially relied mainly on digital rectal examination and rigid proctoscopy, became more accurate with the use of endorectal ultrasound, CT scan and MRI. CXRT was also used for local control in association with external beam radiotherapy (EBRT) and sometimes in association with concurrent chemotherapy for inoperable elderly patients with T2 and early T3 tumors (less than 5 cm in diameter) It was possible to achieve long-term control in 80% of T2N0 tumors and 50% of early T3 tumors [7,8]. A randomized trial, including T2 and early T3N0 tumors of the low rectum, was initiated in Lyon (France) to compare in a preoperative strategy EBRT alone with CXRT + EBRT. This trial demonstrated a significant improvement of clinical complete response (29 vs 2%) and of sphincter-saving surgery (70 vs 30%), which was maintained after 10 years of follow-up [9].

Despite these excellent results, CXRT was abandoned mainly because after 1985 the Philips Company interrupted the manufacture of the Philips RT50 during a period related to the development of linear accelerators, which was the major field of interest of the radiotherapy industry. With the shortage of the Philips CXRT units and the development of endoscopic local excision of T1N0 tumors by surgeons or gastroenterologists, there were increasingly fewer patients who were suitable candidates for CXRT

 10.1586/ERD.11.28 ISSN 1743-4440

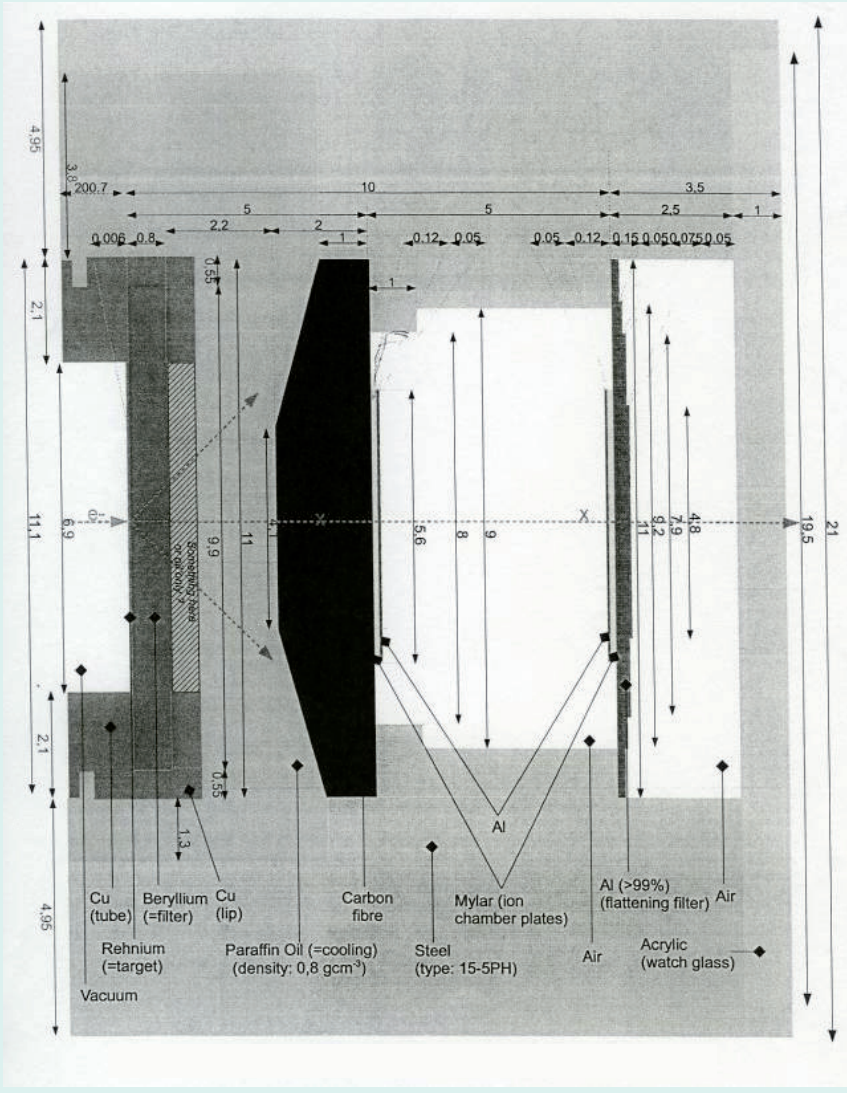

Figure 1. Schematic of the distal part of the x-ray source (Micronode™) of the Papillon 50™ system. Values in millimetres; scale 12/1.
Provided by Ariane Medical Systems.

and the clinical expertise of this approach was lost. It was only in a few departments in France, England and the USA [6,10,11] that CXRT was used for rectal cancer.

Attempts & success for a renaissance of CXRT in rectal cancer

Since the early 1990s it was clear that there was no future for this technique without a new CXRT machine. Efforts were made in Lyon to find a 50 kV machine able to mimic the Philips RT 50 and also able to deliver in a short time (in few minutes) a high dose (20–30 Gy) directly through a rigid rectoscope on to the rectal tumor under direct visual control. Some experiments were made with the Intrabeam™ machine, at that time manufactured by the US Photoelectric company. It was a failure because the dose rate was too low and the tube too short to reach the rectal tumor. Fortunately, in 2004 Ariane Medical Systems took interest in the design of a new CXRT machine suitable for rectal cancer. The unit was designed and assembled in England along with the risk analysis and all financial, industrial, administrative work to gain CE marking, which was finally obtained in 2008. The first machine was delivered to the department of Sun Myint in 2009 in Clatterbridge and the first patient with rectal cancer treated on 15 October 2009.

Characteristics of the Papillon 50 system

Description of the machine

The tube itself is derived from a 50-kV tube manufactured in Saint Petersburg (Russia). The anode is made of rhenium (atomic number: 75). This rhenium anode is very thin (6 µm) and works as a transmission anode. The tube is cooled using an oil circuit, which allows the machine to dissipate heat and reach a high dose rate. A temperature sensor prevents overheating of the tube by controlling the cooling time. With this approach, the stability in the dose rate was achieved.

The window is made of beryllium (0.8-mm thickness). An ion chamber is positioned near the exit of the tube to monitor the dose. Figure 1 gives a schematic display of the head of the rod and tube called a 'micronode'. The treatment parameters are 50 kV and 2.7 mA.

When it is not used, the tube is stored in a shielded tube. This parking tube can also be used to test the x-ray emission.

With applicators, there is a beam angle of 40° emission. The SSD is different for each applicator, and varies between 29 and 45 mm. Each applicator has a unique ring color code for detection and verification by the software.

Incorporated in the tube (18-mm diameter) is a viewing system made of three optic fibers producing light and a camera, which allows direct online vision of the rectal tumor or rectal mucosa, which is displayed on the screen of the Papillon machine. This viewing of the target, which is mandatory for an accurate irradiation with permanent 'eye vision guidance', can be performed before treatment, when examining the tumor and positioning the applicator and during the whole of the treatment time (which is 1–3 min) to ensure that there is no displacement of the beam.

The assembly of the machine components and the computer assisted unit is carried out in the UK. There is a touch screen. The software has two parts: the clinical mode to treat patients and the service mode for tests and to enter parameters.

For security and safety the machine will not operate without the treatment applicator.

For quality control of the dose rate, a special adaptor is provided to place an ionization chamber near the end of the applicator.

Accessories

Rectal applicators

As the tube (micronode) is only 18 mm in diameter it is possible to design rectal applicators as small as 2.2 cm in external diameter. Experience gained with the Philips machine showed it was possible and desirable to irradiate a larger surface (and volume), therefore larger rectal applicators have been designed. They are made of stainless steel, which can be sterilized in an autoclave. There are three different diameters of applicator: 3, 2.5 and 2.2 cm. Oblique applicators were designed in order to prevent collapse of the normal rectal wall and to better encompass tumors hard to cover with a straight applicator, such as low located tumors. The angle of the oblique end is 30° and there are two diameters of 3 and 2.5 cm, providing a slightly ovoid shape of the beam at the exit of the applicator. The applicators at their proximal end, which will be connected to the body of the x-ray tube, have a specific color ring, which allows the applicator to be identified and makes possible its connection to the machine according to the medical prescription through the control of the computer. This is to avoid any mistake in the use of the appropriate applicator. This control is important as the applicator has a small difference in length, providing a difference in SSD that varies from 4 cm with the 3-cm applicator to 2.7 cm with the 2.2-cm applicator. The dose rate and the percentage depth dose also vary according to the choice of the applicator.

Patient support device & fixation mobile arm

There are some differences between the new P50 and the Philips machine; in the Philips machine the tube was hand held, while the Papillon 50 works with a moving tube and the applicator is positioned manually to place it in contact with the tumor (or the rectal target wall) and then fixed steady through flexible metallic mobile arms attached to the patient support device. The position of the tube is permanently controlled online using the internal viewing system incorporated within the tube. The dose is delivered through the pressure on a pedal switch with the machine being at 1 m from the patient or could be operated remotely from outside the treatment room. In this way, radiation protection of all the persons involved in the rectal irradiation can be achieved.

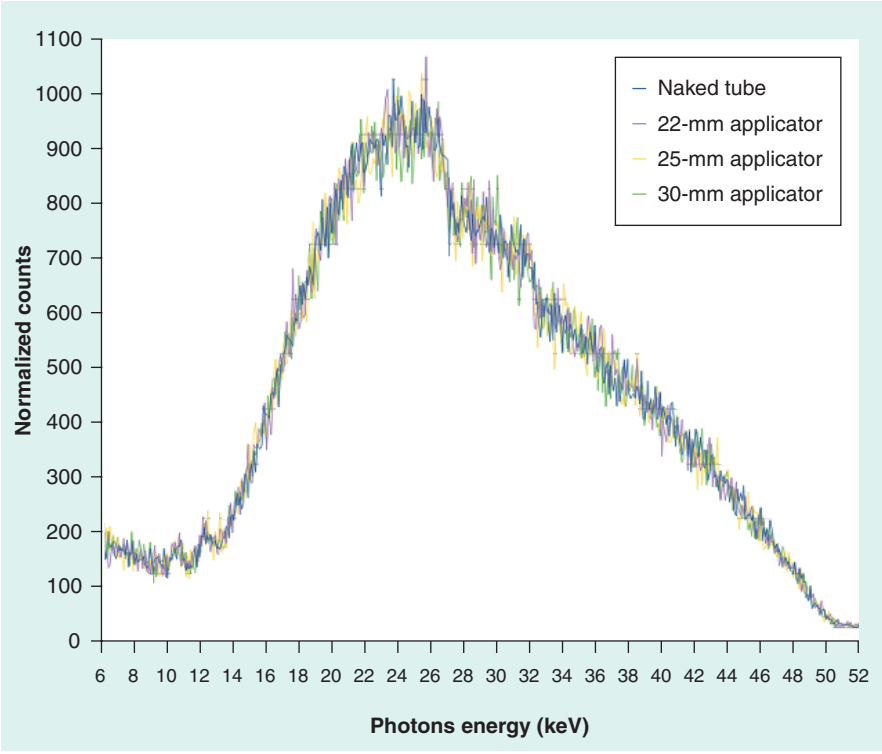

Figure 2. Papillon 50™ x-ray beam spectra measured with a cadmium telluride spectrometer for the three applicators and the naked tube. Curves are almost overlapped. The presence of the applicators does not produce significant changes. Data produced by JM Bordy and C Denoziere from Laboratoire Natural Henri Becquerel, Orsay, France.

Characteristics of the beam

Methods of evaluation

Many physical checks and dosimetric measurements have been carried out to evaluate the performance of the machine and the characteristics of the x-ray beam produced. These measurements were made by the physicists of Ariane Medical Systems and by the physicists of the radiotherapy department in Clatterbridge (UK) and Nice (France). Different ionizing chambers well adapted to 50 kV x-ray beam were used. They were calibrated in reference to the national laboratory standard of the UK and Germany according

Table 1. Dosimetric characteristics of the Papillon 50™ unit measured with two different rectal applicators of 3- and 2.2-cm diameter.

Dosimetric characteristics	3 cm	2.2 cm
FSD (mm)	38	29
Dose rate surface (Gy/min)	20	35
HVL (mm Al)	0.57	0.55
50% depth dose (mm)	7	6.5
Dose at 5 mm (Gy) (10 Gy/surface)	6	5.5
Dose at 10 mm (Gy) (10 Gy/surface)	3.8	3.4

Maximum energy of beam: 50 keV.
Mean energy of beam: 26.5 keV.
Filtration 0.2 mm aluminum – mAs: 2.7
FSD: Focus surface distance; HVL: Half value layer.

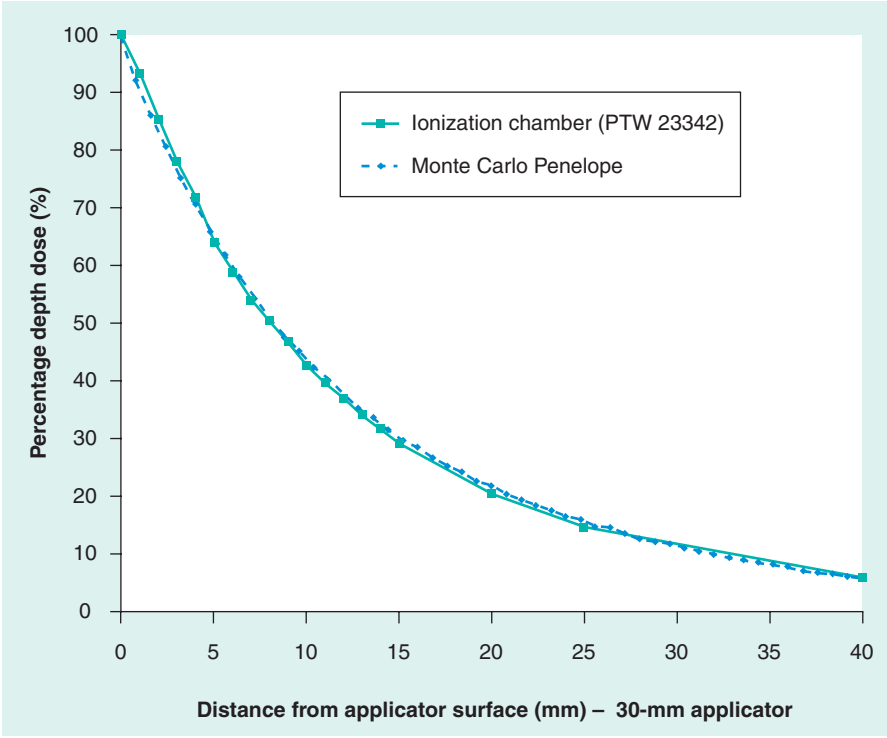

Figure 3. Percentage depth–dose curves for the 30-mm applicator, in a poly(methyl methacrylate) (PMMA) phantom. The dashed curve is related to Penelope simulation and the solid curve is related to the measurements from Physics Technics Wendenhaus chamber.
Data provided by O Croce and already submitted for publication.

to the international recommendation. It is interesting to notice that according to countries some differences can be observed depending on whether the dose or kerma is measured in air or in water. It should be recommended that any medical user of such 50-kV x-rays proceed to a well-validated calibration of the machine and that all Papillon 50 users collaborate toward an international consensus for such a calibration and participate in inter comparison dosimetry tests. A protocol has been developed by the American Association of Physicists in Medicine [12] based on ionizing chamber calibration in air in terms of air kerma. Besides ionizing dedicated chambers and suitable phantoms, Gafchromic films have been used to measured dose profiles. The use of Monte Carlo code is a well adapted method to calculate the different dose distributions achieved with the x-ray beam of 50 kV [13]. In Nice, the use of Monte Carlo code demonstrated a very good correlation between the measurements made with ionizing chamber or Gafchromic films and the simulations made with the Penelope code [Croce *et al.*, Submitted Manuscript, 2011]. Monte Carlo simulations as such could be used to provide atlas files related to the dose distribution of 50 kV r-ray beam. The data can be used to design a reliable method of dose calculation, which can be adapted to a specific treatment planning system for low energies.

Results

Spectrum of the beam

As the beam produced by the Papillon 50 tube is a polychromatic (polyenergetic) beam, it is important to know the distribution and the energy values of the various components of the beam. This spectrometry was performed by the Laboratoire National Henri Becquerel (LNHB) in Saclay, France.

Figure 2 represents the measured spectra of the Papillon 50 x-ray beam for the three applicators and the naked tube. The values have been normalized with coefficients based on the integration of each curve. The curves are all almost identical as they can be superimposed. The maximum energy is near 50 keV and the most probable mean energy for each spectrum is approximately 26.5 keV. These results show that the different size of the applicators does not significantly change the depth dose of the beam. Also, calculation with the Penelope code gave approximately the same spectrum. This beam is closed in its distribution to a standard 50-kV beam (Beam N° CCRI 50b), which is in regular use in the LNHB and which can be used to calibrate the reference ionizing chamber of a physics department. Incidentally the spectrum of the 50-kV x-ray beam produced by the Philips RT 50 in Nice was measured and the maximum energy was found to be only 42 kV, which could partly explain the better depth dose penetration of the 50-kV beam of the Papillon 50.

Stability of the beam

The stability of the beam was tested by the physicists of Ariane Medical Systems. They tested the machine for single runs over 100 h. After a final tuning of the tube, it was found to be fully satisfactory, with a variation of less than 2% over such a long period of time.

Percentage depth dose, half value layer, dose profile & dose rate

All these physical characteristics are of major importance to plan the proper treatment of a rectal cancer and to compare the performance of the beam of the Papillon 50 to other 50-kV machines [14,15]. These parameters change with the type of rectal applicators used. All the measurements were performed in the Department of Physics of Centre Antoine Lacassagne (Nice, France). An overview of these results is shown in Table 1. The University of Nice performed Monte Carlo simulations in order to check and validate the measurements. Again, the comparison of the physical measurements with the results from Penelope code showed a good correlation, as highlighted in the example given in Figure 3. Comparison between the characteristics of the 50 kV beam produced by Philips with RT 50 machine can be seen. It shows that with a 3 cm rectal applicator the Papillon 50 provides a beam with a dose rate slightly lower (15 vs 20 Gy/min), but a better percentage depth dose (50% of the surface dose at 7 vs 5 mm) and a good dose profile at the exit of the tube even with the oblique applicator.

Radioprotection & quality assurance

The radiation leakage from the tube measured was found to be less than 1% in all directions at a distance of 10 cm from the tube. When the tube is mounted with the rectal applicator with the end of the applicator being at 3 cm or more below the surface of the perineal skin (or when a measurement is made in a plastic phantom), the radiation scatter is negligible (less than 10 µSv for 20 Gy delivered at the surface of the tube).

On the contrary, if the tube is positioned on the surface of the skin or of a plastic phantom, the scatter dose is more important. It is 20 µSv at the back of the treatment tube for 10 Gy given to the surface. If one wants to be close to the patient during such an operation, it is necessary to wear lead protection and to monitor the operator dose with an active real-time electronic dosimeter.

From the point of view of room shielding, depending on the national regulations, it is generally stipulated that a 1 mm lead equivalent thickness protection is satisfactory, which is equivalent to 10 cm wall concrete.

Before any clinical use, radiation protection checks must be carried out by the national authority responsible for radioprotection, which will grant the authorization for clinical use.

Acceptance, commissioning, quality assurance & control

As with any new radiotherapy machines installation in a radiotherapy department, acceptance is first performed to validate the main characteristics of the radiation beam and the mechanics of the machine as guaranteed by the industrial manufacturer specifications (Figure 4). Once the machine is accepted, the physics department perform all the measurements and necessary checks before starting the first treatment. Quality assurance requires a dose calibration control every day the machine is used for treatment. The machine is provided with a dedicated phantom used with the reference chamber of the physics department, which makes this measurement fast, reliable and reproducible. As the stability of the beam is satisfactory, the calibration only needs to be modified occasionally. Every year an external audit is performed to verify the characteristics of the machine.

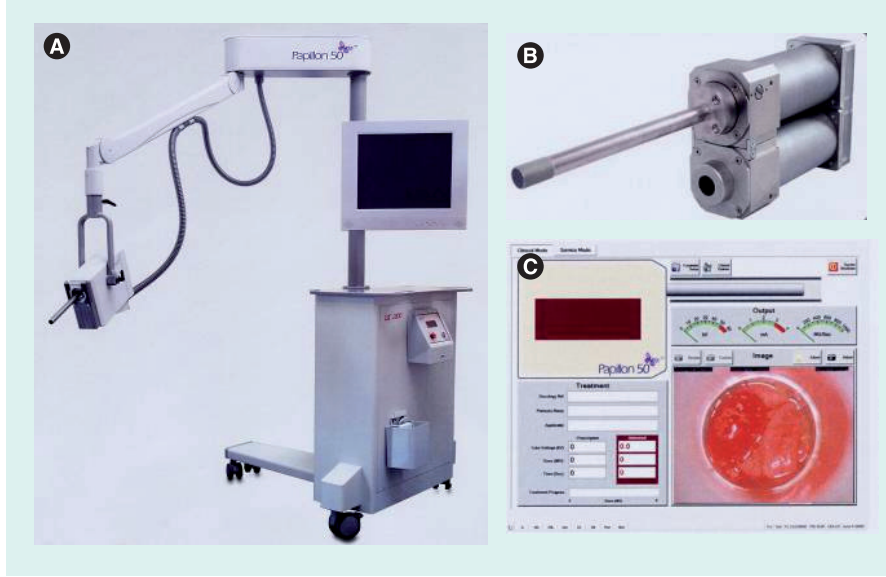

Figure 4. (A) Papillon 50™. (B) Generation and tube (Micronode™). (C) Monitor screen with internal viewing of a rectal tumor.

Description of the procedure for a rectal application

It is in general very similar to the procedure used with the Philips RT 50. The patient is first prepared with an enema to empty rectal ampulla. Examination starts with a digital and rigid rectoscopy. The examination is a crucial step to locate accurately the tumor (or the target site) in the rectum. The proper rectal applicator is chosen and positioned using the external viewing system, which allows the capture of a high-quality digital picture of the tumor (in order to trace and record the clinical tumor response) (Figure 5). When the positioning is satisfactory the applicator is fixed with the mobile arm and the treatment tube is introduced into the rectal applicator. The prescribed dose is then delivered, with operator staying at a sufficient distance from the patient. The internal viewing allows verification during all the treatment that there is no displacement of the tube. When the dose is delivered, the tube and applicators are removed and the patient may be allowed to go home (or go to their room, if they are staying in the hospital). The whole procedure is performed on a fully ambulatory basis.

Compared with the Philips RT 50 the following main advantages can be seen with the Papillon 50. The use of the 3-cm applicator is necessary for tumors more than 2.4 cm in diameter

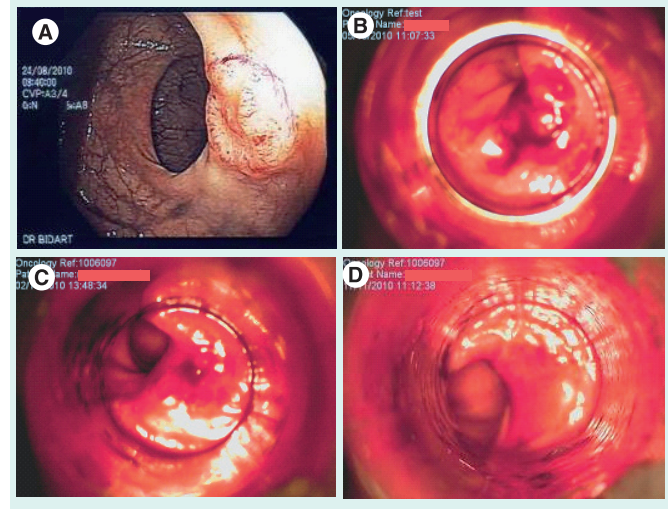

Figure 5. A rectal adenocarcinoma stage T2N0 treated with the Papillon 50™. (A) Endoscope view before treatment (08/2010). **(B)** Image of the tumor seen with the external viewing of the Papillon 50 after first contact x-ray treatment. **(C)** Tumor response with small residual lesion after two sessions (65 Gy). **(D)** Clinical complete remission at end of treatment; total dose: 105 Gy. Patient alive and well with normal bowel movement in April 2011.

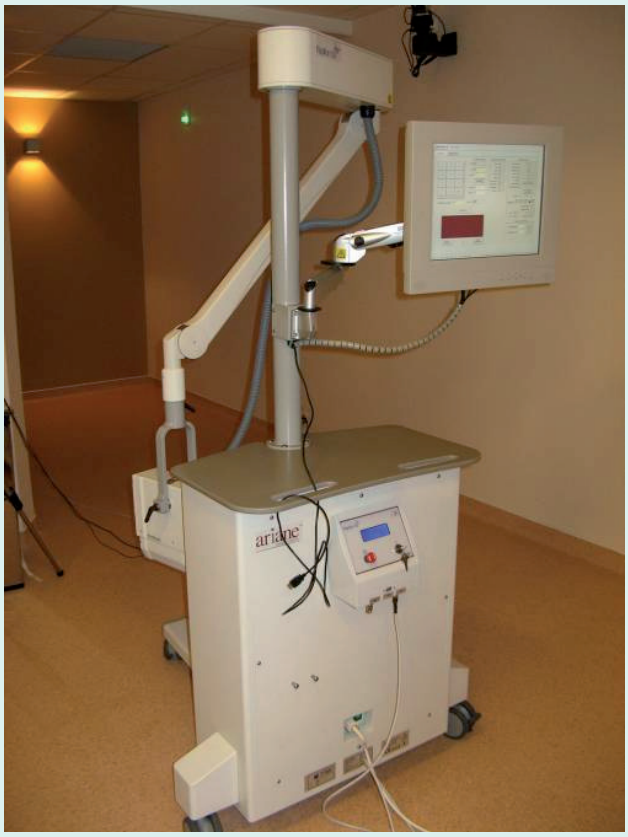

Figure 6. The Papillon 50™ system installed in Centre Antoine Lacassagne. The micronode is stored in the parking stand.

but for smaller tumors or after shrinkage of a large tumor it is always easier and more comfortable for the patient to use the 2.5- or 2.2-cm applicator. The viewing system allows digital recording of pictures of the tumor to document the different phases of the evolution of the tumor during and after the treatment. As the radiation is carried out at a safe distance there is a radioprotection of all the staff involved. As the dose rate is slightly lower with the Papillon 50 and the procedure slightly more complex the duration may be increased by 10–20%. It should be noted that there is no interruption of the irradiation as the applicator is perfectly fixed and its position is constantly checked and controlled.

Clinical applications for rectal cancer & prospective clinical research with the CONTEM trials

The original application of the Papillon 50 is dedicated to rectal cancer. The rationale of its use is related to the capacity to deliver with this technique a very high dose per fraction (between 15 and 40 Gy) with an accuracy of 1 mm under direct visual control. The result is a high rate of local control and little toxicity at any age. Therefore, contact x-ray is used mainly for conservative treatment of rectal cancer. Lesions staged T1N0 can be treated and controlled with CXRT alone or after local excision [1–6]. In inoperable patients T2 and early T3 can be controlled with a combination of CXRT and EBRT [7–11]. One of the new challenges for clinical research is to treat patients with T2N0 lesions with neoadjuvant chemoradiation possibly with the capecitabine plus 50 Gy (CAP50) regimen [16], and to escalate the radiation dose with CXRT in order to safely achieve a complete clinical response [9]. After such a clinical complete response, the patient can be simply followed carefully with digital rectal examination and proctoscopy [17] or submitted to local excision [18,19].

Since October 2009, 125 patients with rectal cancer have been treated at Clatterbridge by Sun Myint and colleagues. Those patients diagnosed with early tumors can be treated with curative intent either after local excision or with CXRT alone. More advanced tumors are treated with chemoradiotherapy initially followed by contact radiotherapy boost in responders. Elderly and frail patients with advanced tumors and nonresponders are often treated similarly for palliation. No significant grade 3–4 adverse events were observed in any of these patients and early clinical results are comparable with the published data. The Papillon 50 will be used clinically for rectal cancer at the end of year 2010 and beginning of 2011 in other departments in the UK, France (Figure 6) and Denmark. After a period of clinical learning experience most of the patients with rectal cancers (Figure 7) will be treated within the framework of three Contact Endoscopic Microsurgery (CONTEM) trials as an international clinical research project [20]. According to the tumor stage (Figure 8) and general condition of the patients the following trials will be considered and activated following informed and signed consent of the patient. They can be briefly described as follows:

CONTEM 1

- Inclusion criteria: patients of any age treated with local excision first for a malignant polyp or early T1 carcinoma less than 2 cm in diameter. If on careful histological examination some adverse features are observed in the pathological specimen, post-excision adjuvant CXRT will be given.
- Treatment : CXRT: 50 Gy in three fractions over 3 or 4 weeks.
- End point: local control expected to be 90% or better at 3 years with no grade 3 toxicity. A total of 80 patients will be included to reach statistical significance.

CONTEM 2

- Inclusion criteria: patients of any age presenting a T2N0M0 adenocarcinoma of the rectum not exceeding 4 cm in diameter or T1N0 more than 2 cm.
- Treatment: CXRT first from day 1 to 28 delivering a dose of 90–110 Gy in three fractions [16] to the gross tumor. EBRT with concurrent capecitabine (CAP 50 regimen) starting on day 21 or 28 and delivering 50 Gy/25 fractions/5 weeks (shrinking field after 44 Gy). An extra dose of CXRT is possible in cases of partial response at the end of EBRT and a local excision will be performed alternatively to 'watch and wait' in cases of suspicious residual disease. Anterior resection will follow in cases of persisting disease R1 or ypT3 on the operative specimen.

- End point: local control (main end point) expected to be 85% over a 3-year follow-up or better with no grade 3 toxicity and good anorectal functioning (Wexner score). A total of 120 patients will be included in order to achieve an α-value of 95% and a β-value of 10%.

CONTEM 3

- Inclusion criteria: T1–2, early T3 (T3a) M0 in inoperable, frail patients.
- Treatment: for T1N0 CXRT alone delivering 90–110 Gy in three-to-four fractions. For T2, early T3 : CXRT 90–130 Gy in four-to-five fractions combined with EBRT. If possible, CAP50 regimen or EBRT alone with a protracted treatment or, if deemed necessary, a short course of EBRT with 5 × 5 Gy in a small volume.
- End point: local control, no toxicity, feasibility of the treatment. As there is no alternative treatment, results will be evaluated without fixed hypothesis regarding local control (Figure 9). An independent data-monitoring committee will regularly analyze the results before the end of accrual.

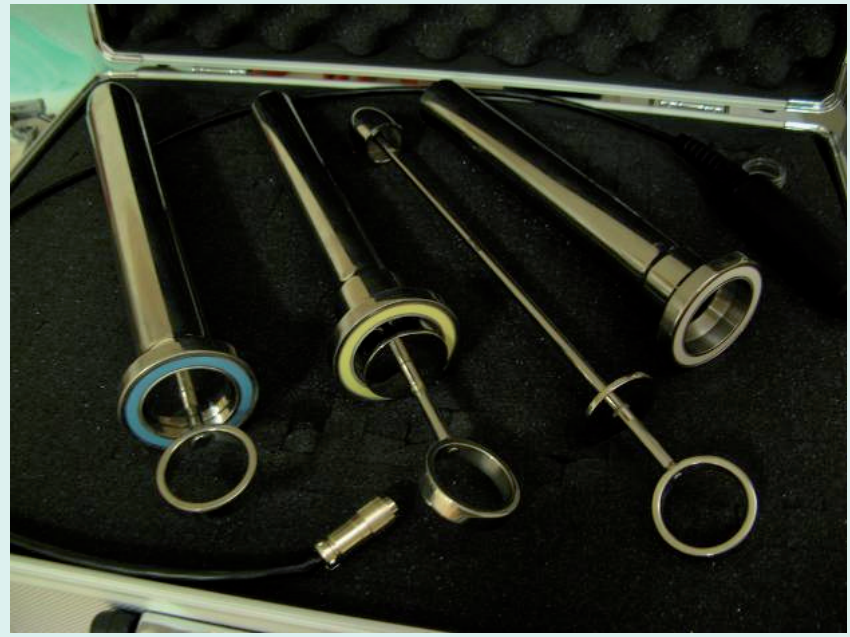

Figure 7. Rectal applicators with color coding for automatic identification by the machine. Three diameters are available: 3, 2.5 and 2.2 cm.

Potential applications for the Papillon systems

- Duplicating the Lyon R96.02 trial and promoting a Phase III trial in low rectal cancer with early T3M0 is under discussion. This will compare neoadjuvant treatment with the CAP50 regimen or other preoperative regimen and the same approach with the addition of CXRT to the gross rectal tumor to increase clinical complete response from 10 to 40% and try to improve sphincter or organ preservation;
- The Papillon 50 can be used to treat skin cancer [21–23], eyelid and conjunctival tumors [24–26]. It can be used for any accessible tumor in a cavity like the vagina [27] or the mouth (Figure 10);
- Intraoperative approach: this is a field of clinical research especially interesting in breast cancer as the Targeted Intraoperative Radiotherapy (TARGIT) trial using the Intrabeam™ machine has demonstrated very encouraging evidence-based results [28]. The Papillon 50 can be used presently to irradiate the retro-areolar plaque during a skin-sparing subcutaneous total mastectomy [29]. It will be adapted with the Nice Breast Applicator to irradiate the tumor bed encompassing three-quarters of sphere after local excision with a dose rate close to 15 Gy/min (Papillon 50BTM).

Figure 8. Applicators used with the Papillon 50™ from left to right: eyelid applicator (1 cm), skin applicator (1, 1.5 cm), rectal straight (2.5 cm), rectal oblique (2.5 cm), rectal straight (3 cm) and rectal oblique (3 cm).

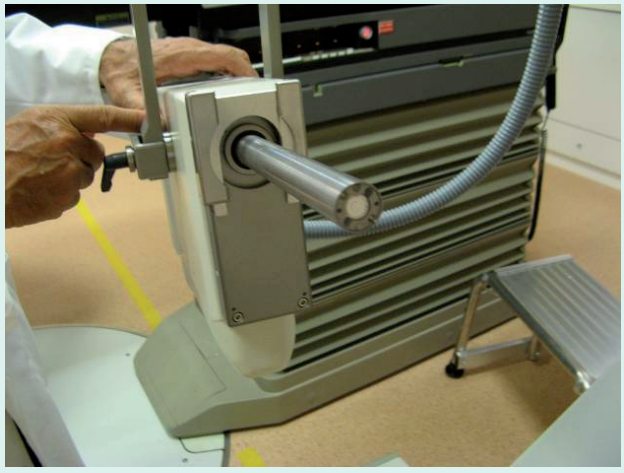

Figure 9. Extremity of the micronode showing the channel for camera, cold light and cooling.

Conclusion

The Philips RT 50 machine is no longer produced. The 'Papillon 50 nouveau' is now commercially available. In an era of global approach for the patient and tailored treatments, the Papillon System provides a good opportunity of clinical use in some selected accessible cancers for the renaissance of CXRT in association with brachytherapy and all modern techniques of EBRT. In future, we hope that the Papillon 50 (or other 50-kV machines) will be available in many radiotherapy departments to treat accessible tumors.

Expert commentary

It is fortunate for the patients suffering with rectal cancer that the new contact x-ray machine Papillon 50 has recently become available on the market. This will allow the renaissance of this efficient, cost-effective and well-tolerated treatment technique. This technique is the only non-surgical treatment to achieve a high cure rate in early rectal cancers with preservation of a normal rectum. Within the frame of the international collaborative clinical trial CONTEM, CXRT will be used in three situations:

- For T1N0 tumors either after local excision or CXRT alone;
- For T2N0 tumors strictly selected with patient at any age to achieve local control with a combination of CXRT, EBRT and concurrent capecitabine;
- For elderly or frail patients presenting with T1, T2 or small T3 to avoid surgical trauma in this vulnerable population.

The radiation oncologist should have some experience with rigid proctoscopy in order to assess the tumor accurately, which is the key issue to achieve optimal results.

Five-year view

It is envisaged that, within the next 5 years, the Papillon 50 machine will enable groups of expert radiation oncologists from the UK, France, Denmark and Sweden to set up and run the CONTEM clinical trials. Approximately 300 patients will be treated and it is hoped that their early rectal cancer will be controlled if not cured with preservation of a well-functioning rectum. It is probable that, in a few years, a good number of new machines will be functioning in Europe, North America and other continents. This will contribute to the renaissance of CXRT and the development of a conservative approach in rectal cancer.

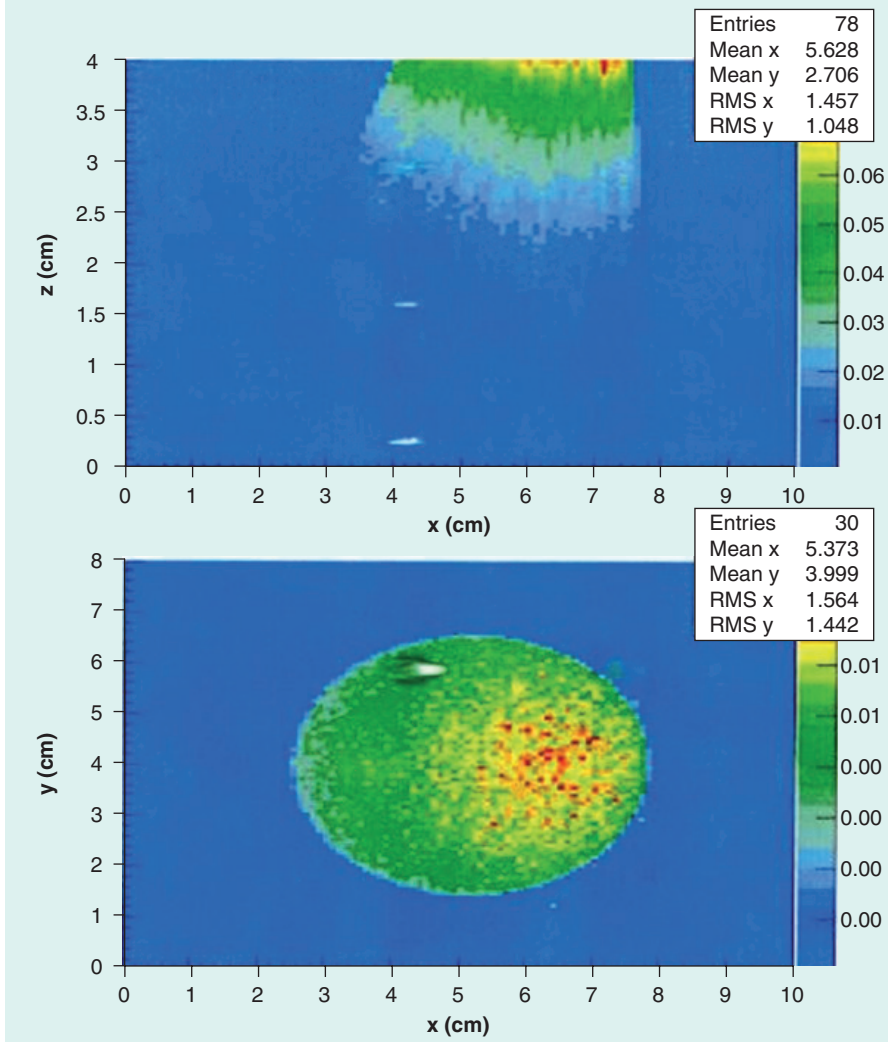

Figure 10. Dose distribution displayed with the MC2 Plan™ software showing the dose inhomogeneity induced by an angulation of 15° of the straight 3-cm rectal applicator. Dose is reduced by more than 10% at the outer part of the x-ray field.

In addition to rectal treatment, CXRT can be used in the treatment of skin, eyelid, eye and breast tumors. Following the results of the TARGIT trial in breast cancer, there is resurgence of interest in intraoperative radiotherapy for breast cancer. The high dose rate of the Papillon 50 machine is an important advantage and will be attractive for breast intraoperative radiotherapy. Finally, as this machine is very cost effective, it could contribute a good deal for clinical use in developing countries.

Financial & competing interests disclosure

*Jean-Pierre Gérard is a clinical advisor of Ariane Medical Systems and receives honoraries. **The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.***

No writing assistance was utilized in the production of this manuscript.

Key issues

- In order to use the Papillon 50™ machine efficiently the radiation oncologist must have good experience in proctology and should be able to use rigid proctoscopy to accurately localize and irradiate the tumor under direct visual control.
- The collaborative international Contact Endoscopic Microsurgery (CONTEM) trial will be a key clinical work to confirm the benefit of CXRT in the conservative treatment of rectal cancer.
- The management of Ariane Medical Systems should be good enough to provide the radiation oncologists with reliable machines.
- A strict quality assurance program involving all the staff of the radiotherapy department should guarantee the safe and efficient use of this new medical device.

References

1 Papillon J. Present status of radiation therapy in the conservative management of rectal cancer. *Radiother. Oncol.* 17, 275–283 (1990).

2 Gérard JP, Ayzac L, Coquard R *et al.* Endocavitary irradiation for early rectal carcinomas T1 (T2). A series of 101 patients treated with the Papillon's technique. *Int. J. Radiat. Oncol. Biol. Phys.* 34, 775–783 (1996).

3 Maingon P, Guerif S, Darsouni R *et al.* Conservative management of rectal adenocarcinoma by radiotherapy. *Int. J. Radiat. Oncol. Biol. Phys.* 40, 1077–1085 (1998).

4 Rauch P, Bey P, Peiffert D, Conroy T, Bresler L. Factors affecting local control and survival after treatment of carcinoma of the rectum by endocavitary radiation: a retrospective study of 97 cases. *Int. J. Radiat. Oncol. Biol. Phys.* 49, 117–124 (2001).

5 Aumock A, Birnbaum EH, Fleshman JW *et al.* Treatment of rectal adenocarcinoma with endocavitary and external beam radiotherapy: results for 199 patients with localized tumors. *Int. J. Radiat. Oncol. Biol. Phys.* 51, 363–370 (2001).

6 Christoforidis D, McNally MP, Jarosek SL, Madoff RD, Finne CO. Endocavitary contact radiation therapy for ultrasonographically staged T1 N0 and T2 N0 rectal cancer. *Br. J. Surg.* 96, 430–436 (2009).

7 Gerard JP, Chapet O, Ramaioli A, Romestaing P. Long-term control of T2–T3 rectal adenocarcinoma with radiotherapy alone. *Int. J. Radiat. Oncol. Biol. Phys.* 54, 142–149 (2002).

8 Myerson RJ, Hunt SR. Conservative alternatives to extirpative surgery for rectal cancer. *Clin. Oncol. (R. Coll. Radiol.)* 19, 682–686 (2007).

9 Gerard JP, Chapet O, Nemoz C *et al.* Improved sphincter preservation in low rectal cancer with high-dose preoperative radiotherapy: the lyon R96–02 randomized trial. *J. Clin. Oncol.* 22, 2404–2409 (2004).

10 Gérard J, Ortholan C, Benezery K *et al.* Contact x-ray therapy for rectal cancer: experience in Centre Antoine-Lacassagne, Nice, 2002–2006. *Int. J. Radiat. Oncol. Biol. Phys.* 72, 665–670 (2008).

11 Sun Myint A, Grieve RJ, McDonald AC *et al.* Combined modality treatment of early rectal cancer: the UK experience. *Clin. Oncol. (R. Coll. Radiol.)* 19, 674–681 (2007).

12 Ma CM, Coffey CW, DeWerd LA *et al.*; American Association of Physicists in Medicine. AAPM protocol for 40–300 kV x-ray beam dosimetry in radiotherapy and radiobiology. *Med. Phys.* 28, 868–893 (2001).

13 Ye S, Brezovich IA, Pareek P, Naqvi SA. Benchmark of PENELOPE code for low-energy photon transport: dose comparisons with MCNP4 and EGS4. *Phys. Med. Biol.* 49 , 387–397 (2004).

14 Beatty J, Biggs PJ, Gall K *et al.* A new miniature x-ray device for interstitial radiosurgery: dosimetry. *Med. Phys.* 23, 53–62 (1996).

15 Fletcher CL, Mills JA, Baugh GM, Roughton J. Comparison of 50 kV facilities for contact radiotherapy. *Clin. Oncol. (R. Coll. Radiol.)* 19, 655–660 (2007).

16 Gérard JP, Azria D, Gourgou-Bourgade S *et al.* Comparison of two neoadjuvant chemoradiotherapy regimens for locally advanced rectal cancer: results of the Phase III trial ACCORD 12/0405-Prodige 2. *J. Clin. Oncol.* 28, 1638–1644 (2010).

17 Habr-Gama A, Perez RO, Sabbaga J, Nadalin W, São Julião GP, Gama-Rodrigues J. Increasing the rates of complete response to neoadjuvant chemoradiotherapy for distal rectal cancer: results of a prospective study using additional chemotherapy during the resting period. *Dis. Colon Rectum* 52, 1927–1934 (2009).

18 Lezoche G, Baldarelli M, Guerrieri M *et al.* A prospective randomized study with a 5-year minimum follow-up evaluation of transanal endoscopic microsurgery versus laparoscopic total mesorectal excision after neoadjuvant therapy. *Surg. Endosc.* 22, 352–358 (2008).

19 Garcia Aguilar J. Pathologic complete response to neoadjuvant chemoradiation of uT2 N0 rectal cancer treated by local excision: results of the ACOSOG Z6041 trial. *J. Clin. Oncol.* 28(Suppl. 7), Abstract 3510 (2010).

20 Lindegaard J, Gerard JP, Sun Myint A, Myerson R, Thomsen H, Laurberg S. Whither Papillon? Future directions for contact radiotherapy in rectal cancer. *Clin. Oncol. (R. Coll. Radiol.)* 19, 738–741 (2007).

21 Caccialanza M, Piccinno R, Beretta M, Gnecchi L. Results and side effects of dermatologic radiotherapy: a retrospective study of irradiated cutaneous epithelial neoplasms. *J. Am. Acad. Dermatol.* 41, 589–594 (1999).

22 Caccialanza M, Piccinno R, Percivalle S, Rozza M. Radiotherapy of carcinomas of the skin overlying the cartilage of the nose: our experience in 671 lesions. *J. Eur. Acad. Dermatol. Venereol.* 23, 1044–1049 (2009).

23 Gerard JP, Coquard R, Rocher FP, Buatois F, Ardiet JM, Romestaing P. The role of radiation therapy for Kaposi disease related to HIV infection. *Nouv. Dermatol.* 15, 35–37 (1996).

24 Schlienger P, Brunin F, Desjardins L, Laurent M, Haye C, Vilcoq JR. External radiotherapy for carcinoma of the eyelid: report of 850 cases treated. *Int. J. Radiat. Oncol. Biol. Phys.* 34, 277–287 (1996).

25 Buatois F, Coquard R, Pica A *et al.* [Treatment of eyelid carcinomas of 2 cmm or less by contact radiotherapy]. *J. Fr. Ophtalmol.* 19, 405–409 (1996).

26 Papillon J, Paufique L, Chassard JL, Hugonnier R, Boyer A, Gérard JP. Contact radiotherapy of epitheliomas of the sclerocorneal limbus. Apropos of 20 cases. *Ann. Radiol.* 14, 609–616 (1971).

27 Schneider F, Fuchs H, Lorenz F *et al.* A novel device for intravaginal electronic brachytherapy. *Int. J. Radiat. Oncol. Biol. Phys.* 74, 1298–1305 (2009).

28 Vaidya JS, Joseph DJ, Tobias JS *et al.* Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): an international, prospective, randomised, non-inferiority Phase 3 trial. *Lancet* 376, 91–102 (2010).

29 Gérard JP, Hannoun-Lévi JM, Raoust I. Contacts x-ray (50 kV) IORT and nipple sparing total mastectomy. *Radioth. Oncol.* 83(Suppl. 1), S42 (2007).