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CT-Guided Brachytherapy Planning

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1. Introduction

Brachytherapy applications are not restricted to one method only; any method could be combined with another, as well as other radiotherapy techniques. In cervical cancer, intracavitary brachytherapy (ICBT) has been used for practical reasons. Lately though, combination of ICBT and interstitial brachytherapy (ISBT) techniques are being evaluated in deference to feasibility, practicality and reproducibility. The possibilities are limited only to the physician's imagination.

Brachytherapy in cervical cancer is indicated in every stage. Currently, general approach is either to operate the patients who have tumors confined in the cervix or treat them with definitive radiotherapy, which consists of BT only or external beam radiotherapy (EBRT) plus BT. The rationale behind is to avoid unnecessary toxicity of surgery and radiotherapy combined in one patient.

2. Historical background

The word "brachytherapy" comes from Latin, meaning "short-distance therapy". That is exactly what brachytherapy is about. Soon after the discovery of radioactive seeds by Becquerel and Curies, radioactive radium seeds were planted inside the tumors. Radiating a target from within outshined delivering the same dose to a target externally in specific tumors. Tumor location, in other words, the accessibility of a tumor made the distinction. First experimentations were done on gynecologic, prostatic and breast tumors. It is not surprising to see brachytherapy approaches still focus on these tumors, as well as other tumor sites such as head and neck, esophagus and in limited cases in lung.

In gynecologic cancers, radiation doses delivered with brachytherapy has been used for more than 100 years. Possibly one of the first presented cases, Margaret Cleaves performed ICBT for cervical cancer in 1903 (Cleaves 1903). Since then, ICBT with or without external radiotherapy has played a major role in curative treatment of cervical cancer. Over the years, application methods as well as dose delivery methods have changed dramatically, reaching a less uncomfortable and much more effective treatment. Among gynecologic cancers, radiation therapy plays a role first and foremost in cervical cancer. Endometrial cancer and vulvovaginal cancers may also be treated with radiotherapy adjunct to surgery. In ovarian cancers, radiotherapy has limited use except for palliative setting.

3. Brachytherapy techniques

Brachytherapy methods can be listed as following:

- *Intracavitary brachytherapy (ICBT)*: Suitable for tumors located in a body cavity, e.g. cervical cancer located at the end of vaginal cavity, or tumors located in the oral cavity.
- *Interstitial brachytherapy (ISBT)*: Where radioactive sources are surgically implanted within the tumor or tumor bed; e.g. breast cancer, tumors floor of mouth or tongue, prostate cancer.
- *Intraluminal brachytherapy (ILBT)*: In which tumors surrounding a luminal organ is accessed via the lumen, e.g. esophageal tumors, lung tumors, biliary tract tumors.
- *Mold brachytherapy (MBT)*: Mold shaped out to fit the target surface is implanted with radioactive seeds, e.g. scalp tumors.

3.1 Dose rates

The dose rate of BT refers to the level or 'intensity' with which the radiation is delivered to the surrounding medium. The dose rate of BT is defined in Grays per hour (Gy/h). In clinical practice, commonly used BT dose rates are as follows:

- **Low-dose rate (LDR) brachytherapy**: Involves implanting radiation sources that emit radiation at a rate of less than 2 Gy per hour (Fu and Phillips 1990). LDR brachytherapy is commonly used for cancers of the oral cavity and oropharyngeal carcinomas (Bourgier et al. 2005; Mazeron et al. 2009), soft tissue sarcomas (Alektiar et al. 2011) and prostate cancer (Koukourakis et al. 2009).
- **Medium-dose rate (MDR) brachytherapy**: Characterized by a dose delivery rate ranging between 2 Gy to 12 Gy per hour (Guedea et al. 2010).
- **High-dose rate (HDR) brachytherapy**: The dose rate is more than 12 Gy per hour. The most common applications of HDR brachytherapy are gynecological cancers (Atahan et al. 2007; Atahan et al. 2008), esophageal carcinoma, lung and prostate cancers.
- **Pulsed-dose rate (PDR) brachytherapy**: Involves short pulses of radiation, typically once an hour, to simulate the overall rate and effectiveness of LDR treatment. Typical tumor sites treated by PDR brachytherapy are gynecological and head and neck cancers.

3.1.1 High-dose rate brachytherapy

Traditionally, cervical carcinoma has been treated with LDR brachytherapy. However HDR brachytherapy was developed to overcome potential disadvantages of LDR brachytherapy, such as unwanted radiation exposure to medical staff, prolonged treatment time, need for long time hospitalization, and possible applicator movement due to prolonged treatment time (Fu et al. 2000). Despite these potential advantages, the primary disadvantage of HDR brachytherapy is the late toxicity due to large doses per fraction, a problem that can be overcome through adequate fractionation schedules. Additionally, in HDR, late tissue complications might be minimized more effectively than in LDR, because greater normal tissue displacement is possible with either packing or some custom made retractors pushing bladder anteriorly and rectum posteriorly (Stitt et al. 1992; Thomadsen et al. 1992). Several studies have compared LDR brachytherapy to HDR brachytherapy in the management of cervical cancer.

Advantages of HDR vs. LDR in cancer of the cervix

- Eliminates undesired radiation exposure hazard to caregivers, visitors; and also diminishes radiation exposure during source preparation and transportation, which may reduce the risk of secondary cancer risk.

- Treatment times are shorter leading to:
 - Less discomfort to the patient
 - Ability to treat high risk patients who are unable to tolerate long period of isolation, such as patients with cardiopulmonary diseases, musculoskeletal diseases, etc.
 - Less risk of applicator movement during therapy.
 - Cost-effectiveness, since there is no need to hospitalization.
 - Larger number of patients treated in institutions that have a high volume of cervical cancer patients but insufficient inpatient facilities (for example, in some developing countries).
- Reduction in the need for heavy sedation or general anesthesia. Since the diameter of sources used in HDR brachytherapy is less than that of LDR brachytherapy, extra dilatation of cervix for insertion of larger sources into cervical os is eliminated.
- Treatment-dose-optimization. The variation of dwell time with the single stepping source allows an almost infinite variation of the effective source strength and source positions allowing greater control of the dose distribution and potentially less morbidity.
- Integration of EBRT and HDR, which can lead to a shorter overall duration of treatment and potentially better tumor control.

Many studies comparing HDR and LDR BT demonstrated comparable local control, survival, and morbidity (Akine et al. 1990; Fu and Phillips 1990; Orton 1991; Teshima et al. 1993; Patel et al. 1994; Petereit and Pearcey 1999), some studies even showed less rectal complications with the use of HDR (Fu and Phillips 1990; Patel et al. 1994). In order to standardize the treatment with HDR brachytherapy, The American Brachytherapy Society (ABS) formed a committee to issue guidelines specifically for the use of HDR brachytherapy for cervical carcinoma in 2000 (Nag et al. 2000).

The ABS recommends that brachytherapy must be delivered during EBRT time, based on the Patterns of Care studies that show that recurrences and complications are decreased when brachytherapy and EBRT were embedded (Coia et al. 1990; Montana et al. 1995). The relative doses given by EBRT vs. brachytherapy depend upon the initial volume of disease, the ability to displace the bladder and rectum, the degree of tumor regression during pelvic irradiation, and institutional preference. Another important recommendation of the ABS is to keep total treatment time less than 8 weeks, because prolongation of total treatment duration can adversely affect local control and survival (Girinsky et al. 1993; Petereit et al. 1995). The recommendation is therefore to interdigitate the implants during the EBRT (but EBRT is not given on the day of HDR). Typically, if the vaginal geometry is optimal, HDR brachytherapy is started after 2 weeks of EBRT. HDR is then continued once a week, with the ERT given the other 4 days of the week. If, due to large tumor volume, it is necessary to delay the start of HDR brachytherapy, it is advisable to perform two applications per week after the EBRT has been completed, so that the total treatment duration is kept within 8 weeks.

The ABS recognizes that the whole pelvic EBRT dose varies from one institution to another. Some institutions prefer to limit the whole pelvis dose for patients with early disease and to perform the first intracavitary insertion after 20 Gy, with further EBRT delivered with a central block in place. The ABS recommends careful attention to the complex matching between the intracavitary system and the edge of the midline block, which is critical to the

success of this approach (Eifel et al. 1995). However, the individual fraction size should be kept to less than 7.5 Gy due to reports of higher toxicity with larger fraction sizes (Orton et al. 1991; Orton 1998).

There is no consensus regarding the use of midline blocks. The ABS recommends that, if used, simple rectangular blocks should routinely be between 4- and 5-cm wide at midplane when intracavitary brachytherapy applicators are used. Optimally, customized midline blocks based on radiographs taken with similar isocenters and reflecting the isodose distribution of the implant should be considered, if possible. When a midline block is inserted before 40 Gy, it should not extend to the top of the pelvic field because it will shield the common iliac and presacral nodes. When there is suspicion of uterosacral ligament involvement, it is safer to avoid early placement of a midline block, which could potentially shield disease posterior to the implant.

The ABS recommends use of multiple HDR insertions to allow progressive tumor volume reduction, allowing more effective disease coverage with the subsequent application. If there are any deficiencies in the initial insertions, adjusting applicator position and packing from fraction to fraction is recommended. Optimum applicator placement and attention to details are critical in both maximizing local control and minimizing complications. The ABS recommends considering placement with ultrasound and fluoroscopic guidance, particularly in patients with altered cervical anatomy because the narrow HDR tandem potentially presents a higher risk for uterine perforation.

It is important to choose an applicator that can optimally treat the disease and can be placed in an anatomically distorted vagina. When tandem and ovoids are used, the largest ovoid diameter that can be accommodated in the fornices without displacement should be inserted. The ring applicator is particularly useful when the vaginal fornices are asymmetric or absent and it is popular because it has a reproducible geometry and is easy to insert. It is important that the plastic caps of the ring applicator be in place with each insertion, because excessive vagina mucosal doses would be delivered without them. It is also important not to activate the entire ring circumference; usually the lateral 4–6 dwell positions are activated on each side of the ring, depending on the ring diameter.

4. Conventional brachytherapy planning

Before going into conformal BT, a short description of conventional BT planning will be given to enable a better comparison. As it is, conformal 3D BT is a result of the need for better treatment modalities.

In the second part of the 20th century, conventional BT planning played a prominent part up until the introduction of imaging techniques to BT in the 1990s. From 1950 to 1990, three major conventional BT planning systems were utilized.

The oldest one, the Paris system consisted of two cork colpostats in the form of a cylinder and an intrauterine tube. A dose of 7000–8000 mg-hrs of radium (Ra) was given in a period of five days. In this system, both the uterus and vagina were treated to similar doses, without any distinction between the tumor and adjacent normal tissues.

The following Stockholm system is where fractionated BT was first introduced. It consisted of 2–3 applications, each taking 20–30 hours. As an improvement after Paris system, uterus and vaginal doses were different, presenting a primitive conformality. In this system, intravaginal boxes and an intrauterine tube were used as applicators. A total dose of 6500–

7100 mg Ra was given, 4500 mg Ra of this by the vaginal box. Both Paris and Stockholm systems had a single line for radioactive sources, reaching to the most proximal end of the uterine cavity to ensure dose ranges in paracervical areas.

In later years, more intricate applicator systems were designed. One of the pioneers in the field, Fletcher designed an applicator system with an intrauterine tandem coupled with two colpostats, which was later improved by Suit and Delclos, respectively (Delclos et al. 1980). This applicator consisted of two ovoid colpostats placed bilaterally to a tandem that reaches to the whole length of the uterine cavity (Figure 1).



Fig. 1. Fletcher-Suit-Delclos applicator consisting of one intrauterine tandem flanked by two ovoids

Another common applicator in use was designed by Henschke, first introduced in 1960 (Henschke 1960). This applicator had the same intrauterine tandem, but instead of ovoid colpostats, a ring colpostat was used to hold the cervix in place (Figure 2).

A recent study comparing these two systems showed that ring applicator was superior to tandem-ovoid applicator in dose distribution (Thirion et al. 2005). Here, an emphasis has to be made. The vital decision in the treatment of cervical cancer is whether brachytherapy is used, rather than how. Experience through skill and imagination is more critical than the choice of applicator (Nag et al. 1999). Hence, current guidelines are not recommending any type of applicator but one that the physician is familiar with.

When Manchester system was introduced in 1938 (Tod 1938) and later revised by Tod and Meredith in 1953 (Tod and Meredith 1953), it brought along a big improvement; a way to determine doses prescribed to points representing the targets. They defined anatomical points that would not change from patient to patient, also were independent on applicators of choice. They observed radiation necrosis in rectum and bladder due to high doses, consequently leading them to define a point corresponding to paracervical triangle, which is accepted as the main limiting factor in irradiation of the cervix. Point A, as they proposed, is 2 cm superior from the mucous membrane of the cervix and 2 cm lateral to the uterine canal. In later years, a second Point B was described, corresponding to parametrial wall, 3 cm lateral to Point A in the same horizontal plane (Figure 3).



Fig. 2. Ring applicator consisting of one intrauterine tandem encircled by a shielded ring.

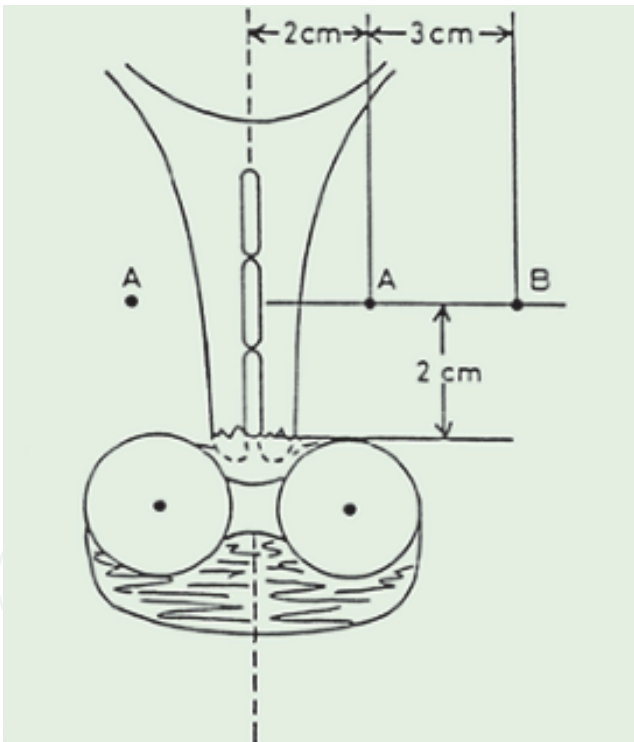


Fig. 3. Point A and B defined by International Commission on Radiation Units and Measurements (ICRU) 38 report published in 1985.

When dose distributions were inspected, it was noticed that Point A was located in a distance where the dose decreased steeply. This fired discussions regarding the reliability of Point A doses, when small changes in applicator placements could result in dire dose differences. In the International Commission on Radiation Units and Measurements (ICRU) 38 report published in 1985, recommendations were made to achieve a common ground in

treating and reporting intracavitary brachytherapy for the cervical cancer. In addition to Point A and B, reference points corresponding to bladder wall, rectum and bony structures were described. The bladder reference point was located according to the Foley catheter inserted into the bladder. The posterior surface of the balloon of the catheter on the lateral radiograph was marked as the bladder reference point. Similarly, posterior vaginal wall was visualized on lateral radiographs; 5 mm posterior on a line drawn at the lower end of the intrauterine source was assigned as the rectal reference point (Figure 4 and Figure 5).

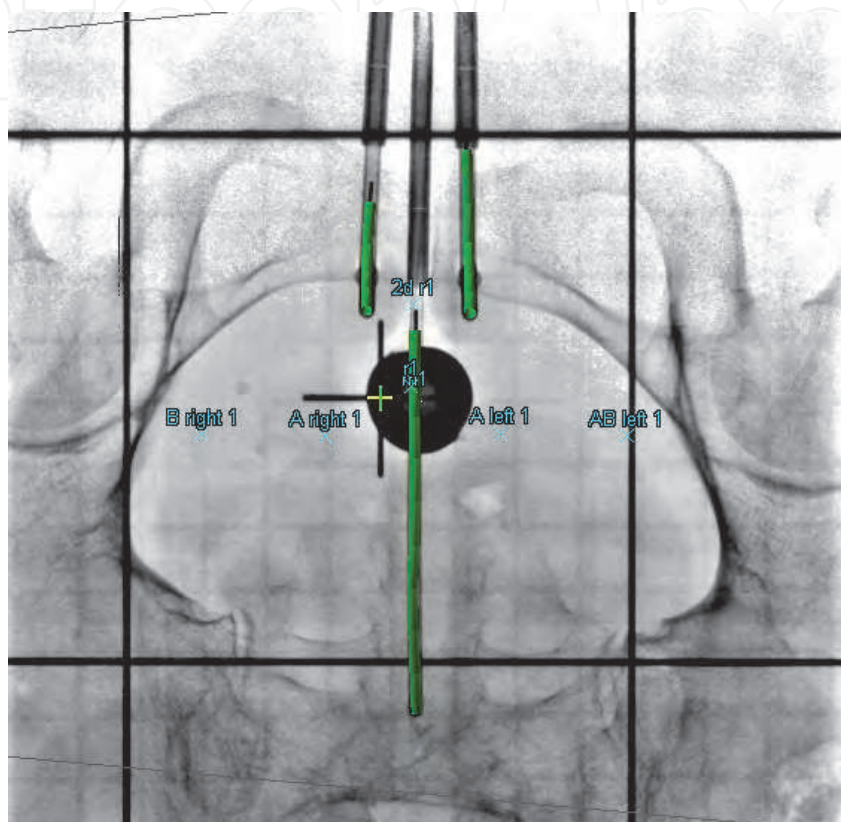


Fig. 4. Bilateral Points A, B, bladder reference point (m1), rectal reference point (r1) on antero-posterior radiograph. Rectal and bladder reference points are superimposed on this image.

The ABS published thoroughly detailed guidelines for intracavitary brachytherapy for carcinoma of the cervix (Nag et al. 2000; Nag et al. 2002). Again, the steep dose gradient where Point A is located was criticized and the many definitions of its location addressed (Nag et al. 2002). To overcome the diversity resulting from these differences, they suggested a detailed description of Point A, as well as other reference points for rectum, bladder and regional lymph nodes.

The main pitfall of the conventional brachytherapy planning stems from its basic idea to determine doses according to reference points which are thought to represent targets. The reference points in conventional BT does not change in accordance with tumor geometry, nor do the reference points for the organs at risk (OARs) in accordance to their respective positions or volumes. An ideal conventional BRT planning with strict respect to the guidelines ensure reproducible and comparable Point A doses between patients. However, that is not to say that each patient has similar dose coverage within their tumor, seeing they each are bound to have

different tumor extensions. What is more, decrease in the tumor volume due to radiation effects presents different target volumes for each BT session. Timing of the BT present another struggle, drawing a line between facing the tumor at its initial size or the possibility of facing a completely recovered cervix at the end of EBRT. In that respect, Point A and B doses offer a false sense of security since both fail to show any undercoverage of the tumor.

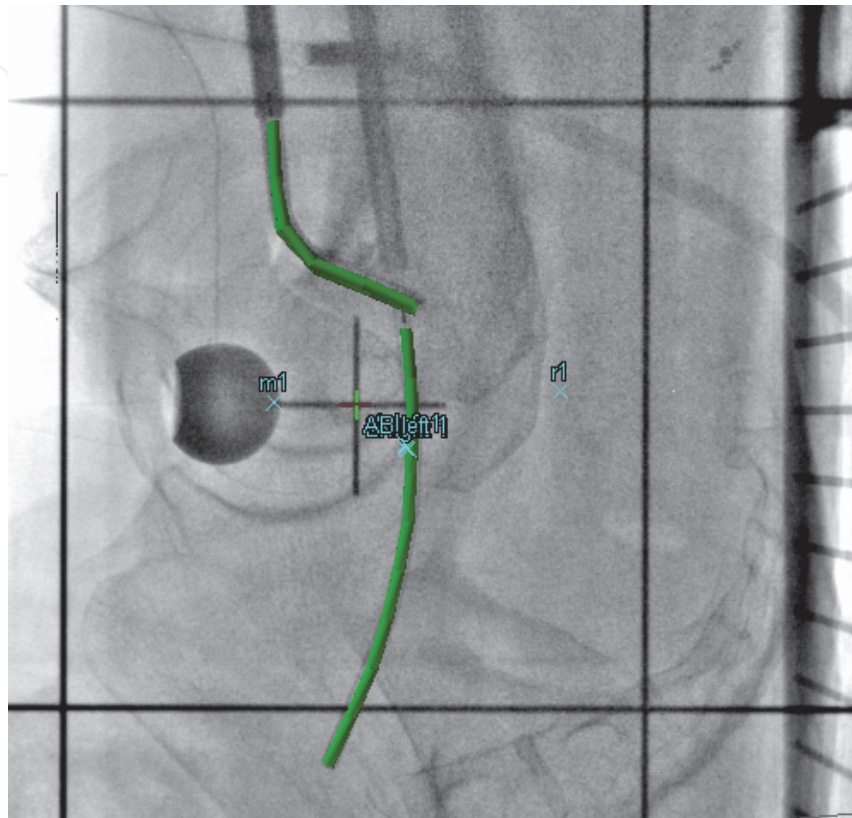


Fig. 5. Bilateral Points A, B, bladder reference point (m1), rectal reference point (r1) on lateral radiograph. Points A and B are superimposed on this image.

Same argument goes for OARs as well. Bladder reference point is reasonably better located, relying on the balloon of the intravesical catheter. This point coincides with the bladder wall, but in conventional BT planning systems, it is impossible to discern if this point is actually within the high dose zone on the bladder. In rectal reference point on the other hand, the point is located according to a visualized vaginal wall border. Except for the experienced eye, it is very hard to make this distinction. Therefore it is possible that the rectal reference point may be located somewhere between the posterior vagina and rectal lumen. Again, it is impossible to know whether this point coincides with the high dose zone within the rectum. In addition, considering both the bladder and the rectum are luminal voluminous organs, trusting a single point to represent the whole organ for every BT session is a big assumption to make.

5. 3D CT-based brachytherapy

Due to target volume irregularities and the close proximity of the target to surrounding organs, such as the rectum, bladder and bowel, it is technically difficult to deliver proper radiation doses to the target volume. It is therefore problematic to achieve a homogenous

radiation dose distribution with conventional 2D plans. Furthermore, it is difficult to assess the organs at risk associated with each dose, especially for doses delivered to the rectum and bladder. The integration of computers and treatment planning systems, especially 3-dimensional (3D) computed tomography (CT) planning techniques, enables easier evaluation of the target volume coverage than previous techniques and allows accurate assessment of the dose delivered to OARs during treatment, which aids in the prediction of toxicity risk (Figure 6). In 3D conformal radiotherapy (CRT), dose-volume histograms (DVH) are delivered for assessment of target volume and OARs doses (Figure 7).

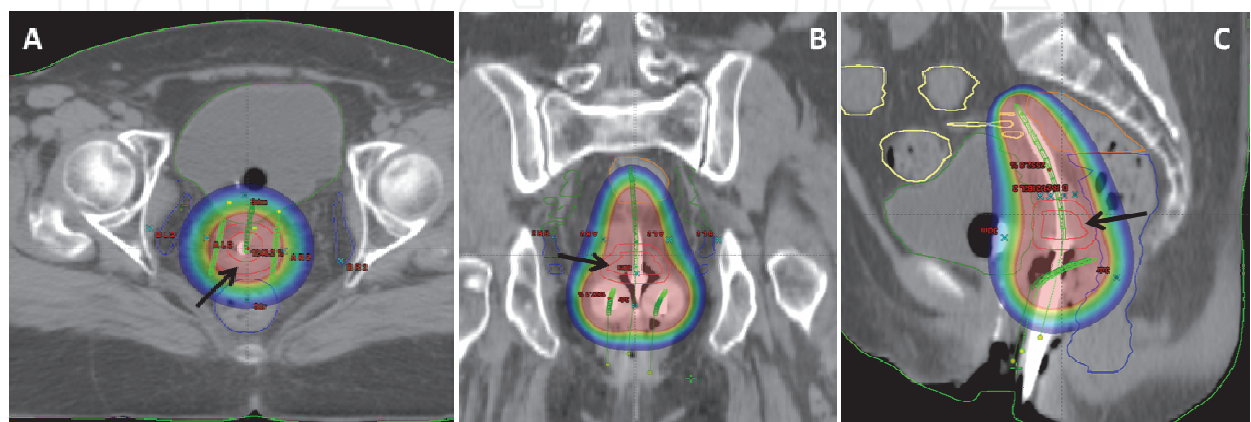


Fig. 6. Dose distribution of brachytherapy application in (A) axial, (B) coronal and (C) sagittal images. The dose is prescribed to target volume (CTV) (arrow). The prescribed dose was demonstrated in red area.

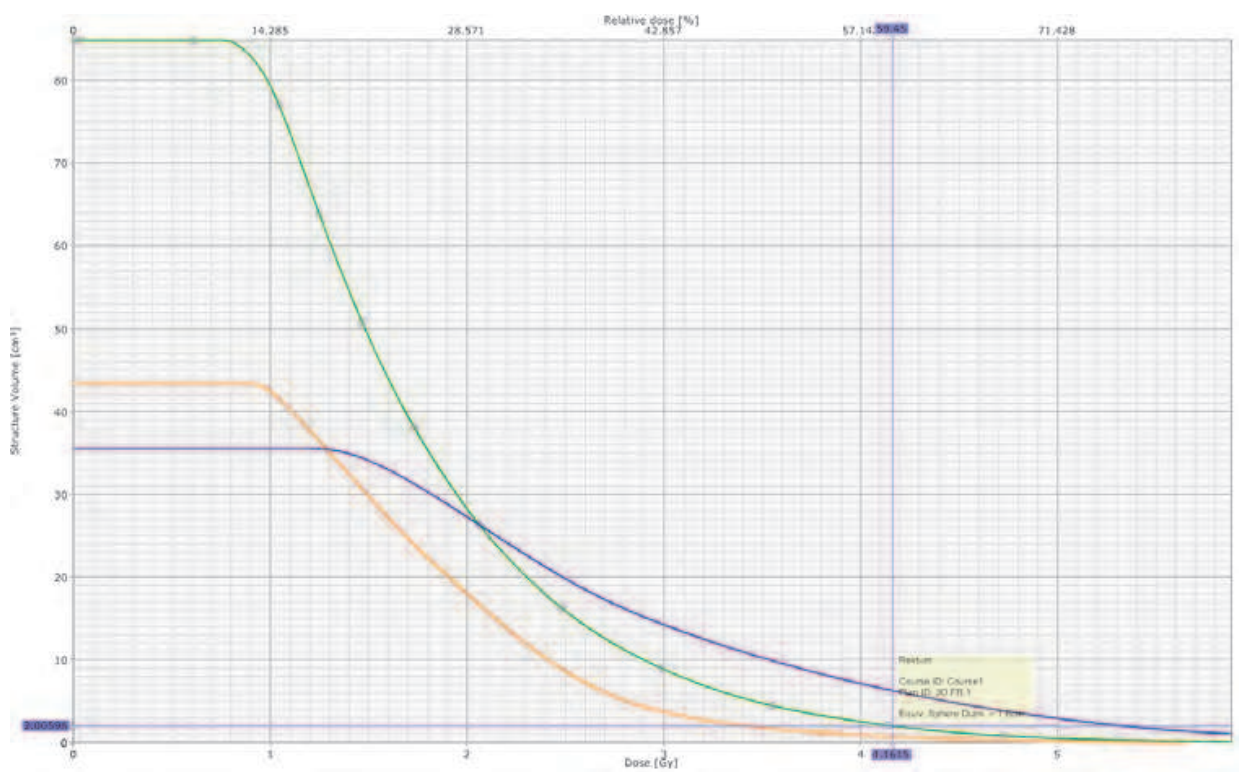


Fig. 7. Dose-volume histogram of a patient demonstrating doses of target volume (orange) and organs at risk (rectum, green; bladder, dark blue).

With the introduction of CT to radiotherapy planning, target delineation have come under spotlight. Instead of indirect ways to calculate doses received by the target, direct visualization of dose distributions within the target volume could be evaluated. What was more; organs at risk could now be delineated instead of assessment through reference points. It was no surprise this renovation happened in the field of brachytherapy. In 1987, Ling published the first CT guided ICBT for gynecological cancers (Ling et al. 1987). In 2004, guidelines were published by Image-Guided Brachytherapy Working Group (Nag et al. 2004). Many studies comparing image based planning techniques with conventional BT planning were published since then (Potter et al. 2000; Wachter-Gerstner et al. 2003; Shin et al. 2006; Onal et al. 2009). The common findings focus around accurate target delineation, better tumor coverage, accurate OARs dose determination and lower normal tissue doses (i.e. rectum, bladder and sigmoid colon). For compared local control and survival data, more studies with adequate follow-up are needed.

5.1 Target volumes

Whether 2D or 3D based, brachytherapy plays a major role in curative treatment of cervical cancer. As in other tumor sites, 3D image guidance in radiotherapy planning has introduced new concepts of gross target volume (GTV) and its derivatives clinical target volume (CTV) and planning target volume (PTV).

For conformal RT, as well as CT-guided BT, some volumes are defined according to ICRU.

- **Gross Tumor Volume (GTV):** Gross palpable or visible/demonstrable extent and location of malignant growth
- **Clinical Target Volume (CTV):** Tissue volume that contains a GTV and/or subclinical microscopic malignant disease, which has to be treated with RT. In fact, CTV is an anatomical-clinical concept, that has to be defined before a choice of treatment modality and technique is made
- **Planning Target Volume (PTV):** Defined to select appropriate beam sizes and beam arrangements, taking into consideration the net effect of all the possible geometrical variations and inaccuracies in order to ensure that the prescribed dose is actually absorbed in the CTV. Its size and shape depend on the CTV but also on the treatment technique used, to compensate for the effects of organ and patient movement, and inaccuracies in beam and patient setup
- **Treated Volume:** Volume enclosed by an isodose surface (e.g. 95% isodose), selected and specified by radiation oncologist as being appropriate to achieve the purpose of treatment. Ideally, Treated Volume would be identical to PTV, but may also be considerably larger than PTV
- **Irradiated Volume:** Tissue volume which receives a dose that is considered significant in relation to normal tissue tolerance. Dose should be expressed either in absolute values or relative to the specified dose to the PTV.

During CT-guided BRT, especially GTV delineation is essential; however either CTV or PTV is preferred for prescribing the radiation doses. Other volumes defined by ICRU are usually used for external beam RT rather than BT.

GTV is considered as one of the important prognostic factor for cervical cancer. However there are still some problems remaining in delineation of target volumes, especially GTV, CTV, PTV. For this reason, there are some guidelines and recommendations made for defining target volumes (Haie-Meder et al. 2005; Potter et al. 2005; Potter et al. 2006).

Accurate delineation of GTV, definition and delineation of CTV and PTV, as well as of critical organs has a direct impact on BT procedure, especially if it is possible to adapt the pear-shape isodose by optimisation allowing DVH analysis for a fixed dose and/or a fixed volume.

GEC-ESTRO decided in 2000 to support and promote 3D imaging based 3D treatment planning approach in cervix cancer BT. A Working Group (WG) was founded (Gynaecological (GYN) GEC-ESTRO WG), which was based on contribution of physicians and physicists from different centers actively involved in this field at that time. The task was to describe basic concepts and terms for this approach and to work out a terminology which would enable various groups working in this field to use a common language for appropriately communicating their results.

In order to take into account major concepts that are basically different and solve the problems in delineating the target volumes, but have both a significant clinical background, two CTVs are proposed by GEC-ESTRO WG:

- A '*high risk*' CTV (HR CTV): with a major risk of local recurrence because of residual macroscopic disease. The intent is to deliver a total dose as high as possible and appropriate to eradicate all residual macroscopic tumour.
- An '*intermediate risk*' CTV (IR CTV) with a major risk of local recurrence in areas that correspond to initial macroscopic extent of disease with at most residual microscopic disease at time of BT. The intent is to deliver a total radiation dose appropriate to cure significant microscopic disease in cervix cancer, which corresponds to a dose of at least 60 Gy.

In, 2004 The Image-Guided Brachytherapy Working Group, consisting of representatives from the Gynecology Oncology Group (GOG), Radiologic Physics Center (RPC), American Brachytherapy Society (ABS), American College of Radiology (ACR), American College of Radiology Imaging Network (ACRIN), American Association of Physicists in Medicine (AAPM), Radiation Therapy Oncology Group (RTOG), and American Society for Therapeutic Radiology and Oncology (ASTRO), proposed guidelines for image-based brachytherapy for cervical cancer (Nag et al. 2004). The Working Group proposes that the primary GTV be defined through imaging (GTV_i) plus any clinically visualized or palpable tumor extensions. This volume is meant to include the entire determinable tumor (the primary tumor in the cervix and its extensions to the parametria as determined by MRI plus the clinical examination). Because the actual target volume for ICBT remains uncertain, the GTV_{cx} is defined as the GTV plus the entire cervix. If the entire cervix is involved by tumor, the GTV and GTV_{cx} will be the same.

In 2003, the study group from Vienna University Hospital published their comparative evaluation of radiograph based BT plan versus CT and MR guided planning (Wachter-Gerstner et al. 2003). As one of the older schools practicing 3D image based brachytherapy, they also marked the differences between the three modalities. They introduced a parameter for conformity; a relation between the 95 % isodose volume and target volume. MRI based BT plans presented statistically significant conformity compared to radiograph based plans without any increase in the bladder and rectum doses. In the patients who had both CT and MRI at the beginning of BT, they found that target volumes delineated on CT images were 1.2 times larger than the volumes delineated on MRI images. Consequently, MRI plans enabled dose escalation compared to conventional plans by a factor of 1.38. In CT plans, this factor was 1.24. They were also

one of the first groups that mentioned the need for interstitial brachytherapy, based on the fact that individualized dose distribution was limited by intracavitary BT only, particularly in patients with parametrial extension.

Shin et al. evaluated 30 brachytherapy plans in 2006 (Shin et al. 2006). To run a thorough comparison between conventional and CT based BT planning, they used the following entities: Coverage index (CI) is the fraction of target receiving a dose equal to or greater than the reference dose. External volume index (EI) is the ratio of the normal tissue volume outside the target receiving a dose equal to or greater than the reference dose. Conformal index (COIN), which was first introduced by van't Riet and Baltas (van't Riet et al. 1997; Baltas et al. 1998), is a formulation related to the ratio of CTV volume receiving the reference dose. In an ideal plan, it should be equal to 1 and best dose distributions are achieved when COIN is nearing to 1. In their report, they classified the patients into two groups; 20 patients were in Group 1 where the 100% reference dose (V_{ref}) to Point A fully encompassed the CTVs, and 10 patients were in Group 2, where the 100% reference dose to Point A failed to encompass the CTVs. They found that Group 2 CTVs were significantly larger than Group 1. Upon a closer look, all patients' pretreatment MRI findings and tumor diameter were similar; meaning Group 2 consisted of patients with poorer response to external radiotherapy. They found that V_{ref} for all patients and Group 1 was significantly reduced in CTV plans. CI of the CTV plan for all patients and Group 2 patients were better than conventional plan. EI was reduced in CTV plan for all patients and Group 1 patients. Similarly, COIN for all patients and Group 1 patients were greater in CTV plan, which corresponds, as expected, to higher conformity. As for OAR doses, their comparison yielded interesting results. They ascertained that conventional planning underestimates maximal bladder and rectum doses, both of which were significantly reduced in Group 1 patients with CTV plans. In their analysis, Group 2 patients (i.e. patients with larger CTVs) had significantly higher bladder and rectum volumes receiving 50%, 80% and 100% of the reference dose. They discussed the reason for this lack of decrease comes from the reference isodose line covering an irregularly shaped, large CTV, especially in lateral directions to meet parametrial extension. They emphasized that even if the conventional plan has lower mean OAR doses, it fails to cover the CTV to the full, thus resulting in cold spots particularly in parametria, consequently leading to local failure (Petereit and Pearcey 1999; Katz and Eifel 2000).

Closely following this report, Datta et al. published their comparative results (Datta et al. 2006). They pointed out that despite the common acceptance of ICRU 38 reference doses; these point doses were usually not reported (Potter et al. 2001). In their assessment they found that in larger tumors, particularly those with parametrial extension, conventional planning failed to fully cover the tumors. 100% coverage of the tumor ranged from 60.8% to 100%, with tumor volume at the beginning of the ICBT being inversely related. Again, they emphasized the underestimation of ICRU 38 maximal bladder and rectum point doses in light of literature even with large patient numbers (Katz and Eifel 2000).

In a similar study done by this group, Onal et al. evaluated 62 plans in 29 patients comparing conventional plans with CT based plans (Onal et al. 2009). The authors classified the patients into two groups on the basis of whether the 95% isodose line to Point A dose encompassed the CTV or not. The mean percentage of target coverage decreased with increasing tumor size and stage, especially in patients with vaginal or parametrial extensions. The mean percentage of GTV and CTV encompassed within Point A isodose level was 93.1% and 88.2%, respectively. According to guidelines, the minimum

dose in the 2 and 5 cc volumes receiving the highest dose (D2cc and D5cc) for rectum and bladder were calculated. On the matter of whole organ volume versus organ wall contouring in assessing rectal and bladder doses, D2 provides a reliable value, since D2 for the whole organ volume is almost the same as the D2 for the organ wall, which represents the tissue exposed to the highest dose. The clinical importance of D5 in predicting fistula formation has been previously published (Cengiz et al. 2008). In this analysis, the mean D2 and D5 rectum doses were 1.66 and 1.42 times higher than the mean ICRU rectum dose. Likewise, the mean D2 and D5 bladder doses were 1.51 and 1.28 times higher than ICRU bladder dose, all statistically significant. In addition to rectum and bladder doses, sigmoid colon and small bowel have been shown to receive substantial dose (Kim et al. 2007). In their study, they demonstrated that the sigmoid colon received the highest mean D2 followed by small bowel and rectum. In the previous study, this group had revealed that the D2 for the small bowel was higher than D2 for sigmoid colon, and that both D2 and D5 doses for the sigmoid colon were significantly higher in larger tumors.

6. Conclusion

External RT together with ICBT are essential components in treatment of inoperable cervical cancer. With developing technology, especially integration of computer into treatment planning systems, either CT or MRI based treatment strategies both in external RT and BT achieves higher doses to target volumes and lower doses to surrounding organs, resulting in higher local control without increasing toxicities. For this reason, CT is essential for delivering better and homogenous dose distribution, which enables optimal treatment outcomes (Figure 8).

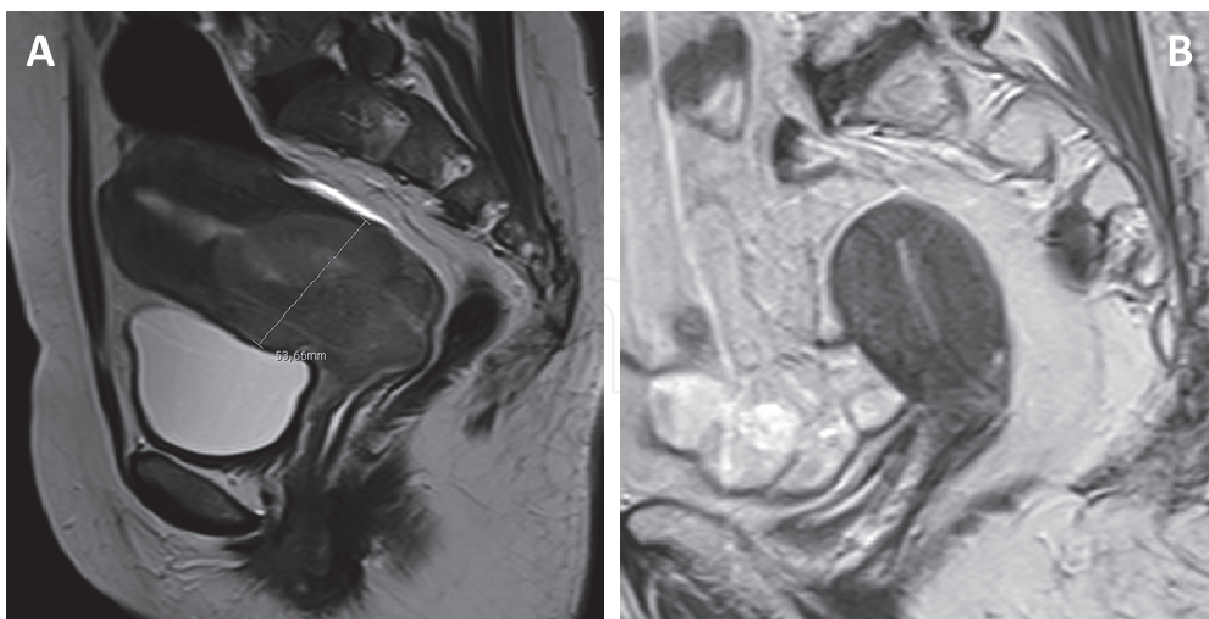


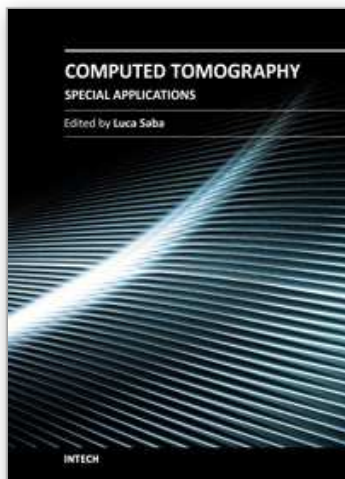
Fig. 8. (A) Magnetic resonance images of a corresponding patient demonstrating bulky tumor before treatment. Large cervical mass located in cervical os infiltrating the parametria and upper portion of the vagina. (B) Complete response after external RT and intracavitary brachytherapy.

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