

Original Article

Brachytherapy in Belgium in 2018. A national survey of the brachytherapy study group of the Belgian Society for Radiotherapy and Oncology (BeSTRO)

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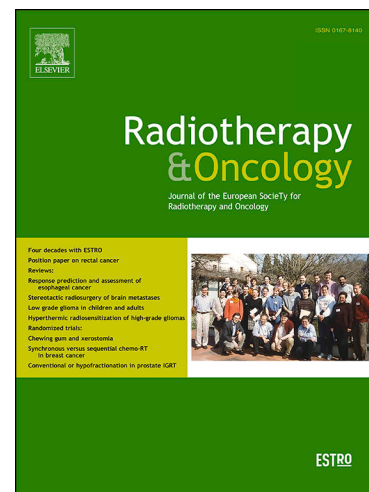
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Brachytherapy in Belgium in 2018. A national survey of the brachytherapy study group of the Belgian Society for Radiotherapy and Oncology (BeSTRO).**Introduction/Purpose**

External beam radiotherapy (EBRT) and brachytherapy (BT) are the two types of radiotherapy techniques that are used clinically [1]. In BT, the radiation device is placed within or close to the tumour or target volume and irradiates internally by means of isotopes. The integration of man-made radioisotopes and remote afterloading techniques has diminished or even completely banned radiation exposure hazards. Innovative imaging modalities (computed tomography, magnetic resonance imaging, ultrasound) and sophisticated computerized treatment planning systems contribute to achieve an increased positional accuracy and an optimized dose distribution [2-4].

The efficacy of BT, as compared to EBRT, is attributed to the ability of radioactive implants to deliver a higher concentrated radiation dose more precisely to the target volume. This might contribute to an improved local control. The steep fall-off of the dose, typical for BT, implements a better sparing of the surrounding healthy tissues. However, in contrast to EBRT, BT often needs an invasive procedure to insert site-specific applicators or to implant specific BT-needles or catheters under sedation or local or even general anesthesia. On the other hand, in many cases BT can be performed on an outpatient basis, avoiding the need for an overnight stay in the hospital. BT also requires very short treatment times; it might be delivered as monotherapy (in one fraction) or in a limited number of fractions (typically 2 up to 5). The patients' recovery time after a BT is usually very short which enables the patients to return to everyday activities or work very quickly.

BT is now been used for over a century. It is a very effective and safe treatment in experienced hands but success is highly operator-dependent as it requires radiation oncologists with advanced technical skills and (some) surgical knowledge. In addition, the brachytherapist needs a well-functioning and well-trained multi-disciplinary team (physicists, technologists, nurses) to cooperate closely.

Notwithstanding the fact that BT demonstrated a remarkable legacy of success over the last century, a disturbing trend of decline in BT use has been reported [5-8]. This decrease in the international utilization rates of BT has also been documented in Belgium. Data from the

Belgium Health Care Knowledge Centre (KCE) show a dramatical decrease in the number of BT treatments of almost 50% between 2007 and 2019 [1]. (Table 1)

In this article we will analyse the results of a survey that was conducted with the aim to evaluate the actual BT resources and the current practice patterns in Belgium.

Material and methods

The survey questions were set up by the Brachytherapy Study Group on behalf of the Belgian Society of Radiation Oncology (BeSTRO) and were based on the online questionnaire that was used by the Brachytherapy Study Group of the Italian Association of Radiation Oncology (AIRO) in 2016[10]. The original AIRO questionnaire, written in Italian, was translated in English without modifications and this 21 questions survey was sent out to all heads of the radiation oncology departments in Belgium.

Our questionnaire contained 21 questions divided over four different sections. In summary:

- Section 1 (Q1-5): background information.
- Section 2 (Q6-16): information on BT equipment and human resources.
- Section 3 (Q17-18): information on the BT procedures.
- Section 4 (Q19-20): information on BT assessment, i.e. the number of patients treated in 2018 for different tumor sites.

Results

All 24 Belgian radiation oncology centers filled-in the questionnaire over a 1-month period (100% response rate).

We obtained information of all (24) primary radiation oncology centers (7 university and 17 non-university centers) as well as of 4 affiliated satellite centers in Belgium. Answers and results from the satellite centers were aggregated in the global result of their primary radiation oncology center.

Four out of 24 centers (17%) answered not to have a BT facility. The other 20 centers

declared to perform various types of BT treatments: 5 centers (21%) only LDR (seeds) BT, 5 centers (21%) only HDR/PDR afterloader BT and only 10 centers (42%) have a full BT facility (seeds + HDR/PDR). (Figure 1)

Eighteen (18) BT afterloader units were functional in Belgium in 2018. Twelve centers only have one type of BT afterloader (11 centers have 1 HDR-afterloader and 1 center has a PDR-device), three centers have two BT units (1 HDR and 1 PDR afterloader). Both (classical) distributors of afterloading units, Varian® (Varian Medical Systems, Inc., Palo Alto, CA) and Elekta® (Elekta AB, Stockholm, Sweden) are almost equally represented in regard to the afterloading units as well as to the dedicated Treatment Planning Systems (TPS). All HDR- and PDR-afterloaders in Belgium use a single stepping ^{192}Ir -source. The number of source-changes per year was also evaluated in this questionnaire. Half of the centers (9 out of 18) perform 4-source changes/year, 44% have only 3 changes/year and 1 center (6%) still has 5 changes/year.

With regard to LDR (seed) BT, as noted, fifteen centers are performing seed BT: 13 centers have a prostate seed implant program, one center has a prostate and eye plaque program and one center has only an eye plaque program. For prostate LDR BT, most centers (86%) are using Variseed TPS (Varian Medical Systems, Inc., Palo Alto, CA).

Analyzing the human resources figures obtained for 2018, a total of 45 radiation oncologists (out of a total of 146 licensed and actively working radiation oncologists) are in some way involved in BT procedures. However, the workload per brachytherapist varies tremendously among hospitals. In some hospitals with a rather huge BT-working load, only one brachytherapist is in charge; while in others, two to four of them performed together a total of 10 to 25 procedures.

A same observation is seen in regard to the physicists involved in BT. A total of 45 medical physicists (out of a total of 110 licensed and actively working physicists) answered to be involved in BT procedures. However, also here, the workload is very different per department. In all departments a minimum of two physicists is related to BT. In some hospitals however, all working physicists seem to be implicated in BT.

The implementation of other medical specialists was reported as very low with the exception of urologists (involved in prostate seed programs), anesthetists and gynecologists (involved in intra-uterine BT). Specific analgesia guidelines were reported as available for the patients

undergoing an ‘invasive’ BT procedure.

Almost all BT procedures under local anesthesia are performed in the radiotherapy department and procedures under general/spinal anesthesia are most frequently performed in operation theatres. Only a small portion of the centers performing afterloading BT has a dedicated ward or theatre implemented in or close by the radiotherapy department.

In 2018, 1486 patients received a BT-treatment in Belgium. 28% of these patients were treated by a prostate seed implant in one of the 14 centres, 8 % were treated by eye-BT (Ru¹⁰⁶ or I¹²⁵) in 2 centres and 64% by HDR/PDR BT in 15 different centres.

With regard to prostate seed implants, an average number per center of (only) 30 patients (min. 12 – max. 60) was treated in 2018.(Figure 2) Sixty five percent (65%) of all centres offering a prostate seed program performed less than 30 procedures/year.

Eye-BT is available in two university centres in Belgium. A total of 121 patients was treated in these two centres. Concerning afterloading-BT (HDR or PDR; Figure 3), a total of 947 patients was treated in Belgium in 2018. Table 2 shows patient numbers per tumour category along with the number of institutions where the techniques are employed and the average number of patients treated at each institution. Two indications of afterloading-BT are widely spread over the institutions (gynaecological (with the exception of primary endometrial BT) and skin/keloid, while most others are performed only at a limited number of institutions and in few cases (bronchus, oesophagus, anal canal, penis, intra-operative BT, primary endometrial). Breast BT, only administered in a boost-setting after a course of external beam irradiation, is performed in two centres (one centre performing a considerable high number of cases, the other only two sporadic cases). Prostate HDR-BT is available in one centre in a relative low number of cases and only in a boost- or salvage setting.

About half of the centres having a HDR/PDR facility perform less than 40 procedures/year (min. 9 – max. 216).

Discussion

This study shows the results of a national survey of the current BT status in Belgian radiation oncology centers.

The major strength of the present survey was that all Belgian radiation oncology centers

replied to the questionnaire (response rate of 100%). Hence, the survey represents the complete Belgian BT practice for the year 2018.

The limited number of procedures performed confirms the universally observed negative trend in BT practice. Published evidence on BT-availability and use is scarce. The only available European data on brachytherapy come from a review published in 2013. This review revealed that there were 657 BT facilities in Europe, representing 52% of all radiotherapy centers.[11] However, no European data are available to indicate whether the number of centers offering BT has fallen. Data coming from the United States might give a clearer view. Safdieh et al demonstrated, using the US National Cancer Database, a fall in brachytherapy utilization for low-risk prostate cancer of 12% between 2004 and 2012[12]. Han et al reported a similar trend for treatment for locally advanced cervical cancer. This population-based analysis using the Surveillance, Epidemiology and End Results (SEER) database revealed a concerning decline in BT utilization in the United States from 83% in 1988 to 58% in 2009[13].

For many years now, surgery and EBRT are more and more preferred over BT even for patients presenting with an excellent indication for BT. A number of factors inducing this preference can be cited. Although the presence of an overwhelming literature confirming excellent oncological results and limited side effects in relation to organ-sparing therapy, surgical approach is often proposed to a patient as sole possibility. On the other hand, intensity-modulated radiotherapy (IMRT) and stereotactic radiotherapy (SBRT) are preferred inside the radiation oncology community as they are non-invasive easier to handle and sometimes less time consuming than BT and because the National Institute for Health and Disability Insurance (NIHDI) reimburses these external beam radiotherapy techniques often (much) better in Belgium. Even more, in 2017 the reimbursement of prostate seed BT was cut down by 30% in the frame of a cost saving program. As an example, the actual reimbursement for the procedure of an IMRT-treatment for localized prostate cancer is 4-times higher than the reimbursement for a prostate seed implant procedure (2550 euro versus 637 euro). Last, the reimbursement of the Iridium source in HDR/PDR treatments was also modified with a need of at least ten to fifteen patients treated with one source to get the full reimbursement. As a consequence, several centers decided to stop to offer this treatment option to their patients, resulting in less than 50% of all radiation oncology centers in Belgium to have in their own department the infrastructure to offer the full-range of BT.

The decline in BT during the last decade led to a vicious circle of fewer cases being treated, inadequate use of BT machines, insufficient maintenance of BT skills in the community and in the academic centers and limited (or absent) training for radiation oncology residents. This finally resulted in a suboptimal recognition of the indications for BT and eventually the absence of best clinical practice as described by Lievens et al.[14]. Since registration of new cases, stage and treatment in the national cancer registry happens via multidisciplinary tumor boards, the quality of this practice could be further explored in future work by a thorough analysis of individual files at the national level.

The mean number of patients treated by BT in Belgian centers is lower than the European average of 100 annually[15,16] In the majority of centers, BT was used almost exclusively as primary treatment for low- or favorable intermediate risk group prostate cancer as seed implant or as post-hysterectomy therapy (vaginal vault BT). Intra-uterine BT as a boost after combination radiotherapy-chemotherapy for inoperable cervical tumors was the following most common indication.

With regard to LDR *prostate BT*, a reduction in cases was universally observed over the last years and this despite excellent long-term results either as monotherapy or as combination therapy [16-23. ASCENDE RT showed that men treated with LDR boost were twice as likely to be biochemically failure-free when compared to EBRT alone [24]. Continuous improvement in planning technology and seed placement may help to reduce the noted increased long-term urinary toxicity in combination cases, whilst hoping to maintain the biochemical benefit over EBRT alone [25]. Four years after the publication of this randomized trial, reimbursement of radioactive seeds for this indication is still not considered in Belgium inducing the impossibility to offer this highly curative treatment to Belgian patients. Robotic radical prostatectomies and improving convenience of hypo-fractionated EBRT for low- to intermediate-risk disease, following the different hypo-fractionation trial publications are competing treatment options that may have impacted on referral practice [26-28].

In contrast to the practice and evolution in almost all western countries, HDR BT for prostate cancer is almost not used in Belgium. Only one center is practicing this technique in a boost and salvage setting. A recently published survey showed a significant increase in HDR BT boost numbers with more UK and Irish centers offering this modality in the last 5 years [29]. The use of HDR BT boost is supported by a randomized trial [19] as well as a large number

of single and multicenter trials [30-38]. Biochemical disease-free survival rates of > 90% for intermediate-risk patients and >80% for high-risk patients are reported in the majority of these studies with very good acute and late tolerance. HDR-BT as a boost can be offered to our Belgian patients with complete reimbursement but is unfortunately often substituted by classical EBRT with long-term androgen deprivation therapy despite the documented impaired outcomes. [19,39]

HDR-monotherapy, another promising field in prostate BT, is not available at all in Belgium. As shown in a Phase II randomized study, HDR-BT as monotherapy is a potential alternative to LDR-BT in low risk and favorable intermediate risk prostate cancer.[40]

Salvage (focal or whole gland) HDR-BT is offered in one department in Belgium. Already in 2013, Chen et al demonstrated that salvage prostate HDR-BT for recurrent prostate cancer after previous definitive radiation therapy is an effective salvage modality with relatively few long-term toxicities.[41] Although with shorter follow-up, Belgian data show the same efficacy and low-toxicity following ultra-focal salvage HDR-BT for recurrent prostate cancer.[42] A recently published comparison of efficacy and toxicity outcomes with HDR- or LDR-salvage BT showed that both treatment modalities yield comparable efficacy and toxicity outcomes in patients undergoing salvage treatment for locally-recurrent prostate cancer after primary radiotherapy. [43]

Finally, the number of prostate seed implants performed by individual consultants is noteworthy. The Royal College of Radiologists (United Kingdom) encourages brachytherapists to perform at least 25 cases per year to guarantee the necessary quality level. Our survey showed that almost 60% (8 out of 14) of centers performed less than 25 cases per year and sometimes done by multiple brachytherapists – so the number of cases per brachytherapist per year will even be less in these centers [16].

Gynecological BT, either as part of a primary radiotherapy treatment or exclusive in the post-hysterectomy setting, is well implemented in Belgium in different departments. Vaginal vault BT (VBT) is the most performed afterloading-BT technique. It is mostly used in a monotherapy and outpatient setting. The efficacy and superiority to adjuvant EBRT was shown by the PORTEC-2 study [44]. Initially, both the PORTEC-1 and GOG 99 had demonstrated a decreased risk of locoregional recurrence with adjuvant EBRT for patients with early stage endometrial cancer. Among patients who had disease recurrence, the vagina was the most common location of failure [45,46]. The PORTEC-2 study compared VBT and

EBRT as adjuvant radiotherapy options in a phase 3, randomized non-inferiority trial for high-intermediate risk patients. The goal of VBT is the eradication of potential microscopic disease within the vaginal lymphatics, which are located within 3 mm of the mucosal surface in most patients. The efficacy of VBT relies on close approximation of the vaginal mucosa to the vaginal cylinder applicator. There is exponential dose falloff at increased distances from the brachytherapy source, resulting in high vaginal mucosa surface doses, and much lower depth doses. VBT resulted in similar rates of vaginal recurrence but with lower GI toxicity compared to pelvic EBRT [44]. PORTEC-2 supports the role of VBT to decrease vaginal failure for high-intermediate risk patients, but also patients that are at lesser, but still potentially significant risk of a vaginal failure might benefit from VBT. Some authors published estimates and treatment recommendations based on the available literature to help guide discussions of the benefit of VBT in these groups of patients [47].

Intra-uterine BT represents the second most used afterloading-BT in Belgium. The standard of care for the nonsurgical curative management of stage I to III cervical cancer includes a combination of chemotherapy, EBRT and BT. Dose modelling studies clearly demonstrate that BT achieves the best radiation dose conformity, tumour dose escalation, and sparing of adjacent normal tissues when compared with advanced external beam modalities including IMRT and proton therapy [48]. The implementation of image-guided BT for cervical cancer report impressive local control rates of 100% for stage IB, 96% for stage IIB, and 86% for stage IIIB patients [49,50]. Moreover, a study by Gill et al. using the National Cancer Data Base to analyse the radiation dose-escalation technique that was used in the treatment of 7,654 patients with cervical cancer underlined the superiority of BT over all other techniques (IMRT or SBRT) [51]. The median survival time was 70.9 months for patients who received brachytherapy compared with 47.1 months for those dose-escalated with either IMRT or SBRT as an alternative to BT. The risk of cervical cancer-specific death was significantly higher for women who did not receive BT (hazard ratio of 1.86) despite controlling for several relevant clinical and pathologic factors. Of particular note, the increase in the mortality rate was more pronounced for patients who did not receive BT than for those who did not receive chemotherapy. Without question, BT is an integral part in the treatment of cervix cancer and is, as stated by Tanderup et al. in 2014, not optional but mandatory [52]. All Belgian centers not offering this type of BT indicate a formal reference policy to another center for this part of the treatment.

The use of BT as boost in the adjuvant treatment of *breast cancer* was relatively well developed in the recent past in Belgium. However, the introduction of hypo-fractionated treatment schedules and the implementation of an integrated boost during EBRT made that the use of a BT boost was abandoned in the vast majority of Belgian centers. Our survey showed the routinely maintaining of boost BT for breast cancer in only one Belgian hospital and the sporadic use in another. Surprisingly, not one Belgian center offers accelerated partial breast irradiation (APBI) by BT in low-risk patients, even though phase II studies showed that it was safe and effective [53-55] and a large European prospective phase III study demonstrated non-inferior outcomes to whole breast irradiation [56].

BT also plays a major role in the treatment of *choroidal melanoma* [57] and is used in 2 centers with long and high experience in this field.[58] As an alternative to enucleation, BT with Ru¹⁰⁶ or I¹²⁵ preserves the eye and vision, and offers excellent local control rates and cosmetic outcomes.

Seven Belgian centers have performed BT for *primary skin cancer*. Only one center treated more than 50 cases, the other centers handled only very limited numbers of patients in contrary to the incidence of this pathology. The lack of referral for primary BT from dermatologists and plastic surgeons might reflect the absence of correct and up-to-date knowledge of these specialists' groups in regard to the ability of modern BT to cure skin cancer with minimal side effects and complete preservation of the anatomy [59,60]. Unfortunately, BT is still often only reserved as second-line therapy for patients with surgical contraindications or as adjuvant therapy for (incomplete) resected high-risk lesions. Only eight centers perform BT for *keloids* although high efficacy with almost absent toxicity is reported in the literature [61].

Small numbers of BT are further observed in some Belgian centers in regard to cancer of the anus, esophagus and bronchus, penis or vulva. Although much less frequent, it is reassuring to see that the métier is still present and that these types of BT can be performed in some centers. With good communication and the presence of an open mind for collaboration and referring, patients could eventually receive BT for these less common indications.

Other types of BT have apparently disappeared. BT for head and neck cancer (in primary or salvage setting) or for brain tumors seems to have been abandoned in all Belgian centers. Newer indications have not yet found their application in our country. We mentioned already

APBI and prostate HDR-monotherapy, but also electronic (skin) BT, BT for bladder cancer (i.c. robotic assisted bladder BT) or for primary rectum cancer have not yet been implemented in Belgian practice unless the emerging literature[62,63].

Although multiple patterns of care studies for radiotherapy have been published, reports dealing only on BT are rather scarce and have mainly been published in the beginning of this century. Guedea et al published two important papers with results of a survey of the patterns of care study for BT in Europe [64,65]. The first paper reported on data collected over a period between 1997 and 2002, the second paper on data collected in 2007. Findings from 2007 were compared with the previous reported 2002 data. Detailed data for the Netherlands, subtracted from this global European survey, were also published in the same time-period [66]. Comparison with these data is difficult since these papers are reporting on a historical completely different BT landscape as nowadays. A simple example among many others is the disappearing of manual afterloading with Iridium-wires (still accounting for more than 15 % of all procedures in 2007) [65]. Other publications focused on a specific treatment site in a specific region, of which one of the most important is the already cited publication by Corey et al. in regard to prostate BT [29].

As stated, our questionnaire was based on the recently AIRO-questionnaire [10]. However, even the data reported in this study are difficult to compare or relate to the Belgian situation. The mean number of BT-patients/centre in Italy is significantly higher than in Belgium (around 100 BT-patients/year versus around 75 BT-patients/year) but this might be biased since in contrast to our survey, AIRO had a response rate of only one-third of all Italian radiotherapy centres. In both countries most BT-procedures are for gynaecological cancer (intra-uterine BT and post-hysterectomy vaginal vault BT) and there is a low incidence of breast-BT, also merely as a boost after EBRT whole breast irradiation. In contrast to Belgium, prostate BT is less developed in Italy.

So, this is the report of the first survey on BT in Belgium. The findings described can help us to define the actual status of BT but can also aid to define goals for future developments. Belgian radiotherapy departments often perform BT only in a (highly) selected group of pathologies, resulting in a limited number of patients treated by this technique despite the sufficient availability of BT equipment. (Modern) indications are often not covered; hence

patients do not have regular access to recognized treatment options, possibly leading to inferior oncological outcome. BeSTRO will use the results of this survey to adapt their training program by including more information on BT. They also plan to improve awareness, education, implementation, collaboration and cooperation in the field of BT by further developing the BT-group of BeSTRO and by stimulating their actions. To optimize the use of BT, they will ask the cancer registry to analyze the use of BT per indication in order to communicate the (eventual under-)use to their members.

Disclosure

The authors report no conflicts of interest.

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Disclosure

The authors report no conflicts of interest.

HIGHLIGHTS:

- In 2019, the Brachytherapy Study Group proposed to conduct a survey on behalf of the Belgian Society of Radiation Oncology (BeSTRO) in order to identify current BT practice patterns.
- Response rate to the survey was 100%
- Belgian radiotherapy departments often perform BT only in a (highly) selected group of pathologies, resulting in a limited number of patients treated by this technique despite the sufficient availability of BT equipment.

- Modern indications are often not covered; hence patients do not have regular access to recognized treatment options, possibly leading to inferior oncological outcome.
- BeSTRO will use the results of this survey to stimulate improvements in training, awareness, education, implementation, collaboration and cooperation in the field of brachytherapy.

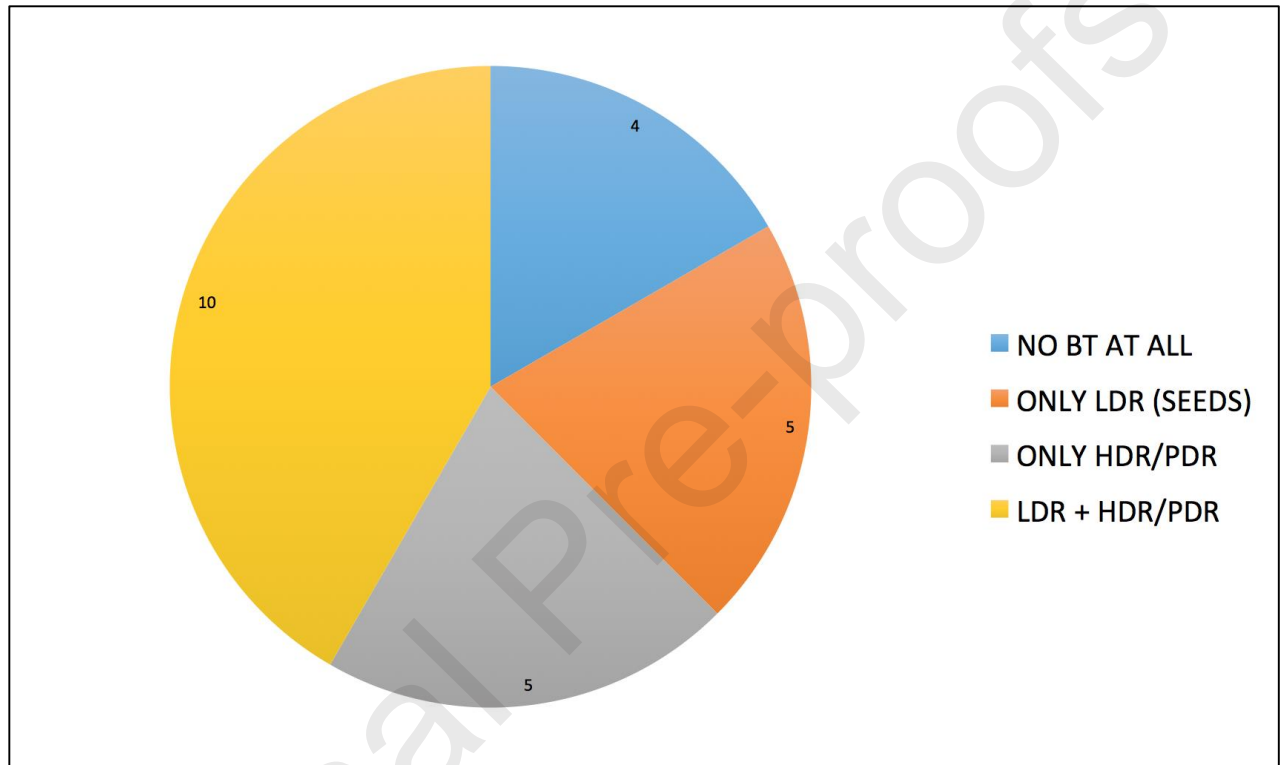


Figure 1: Brachytherapy facilities in Belgian radiation oncology centres

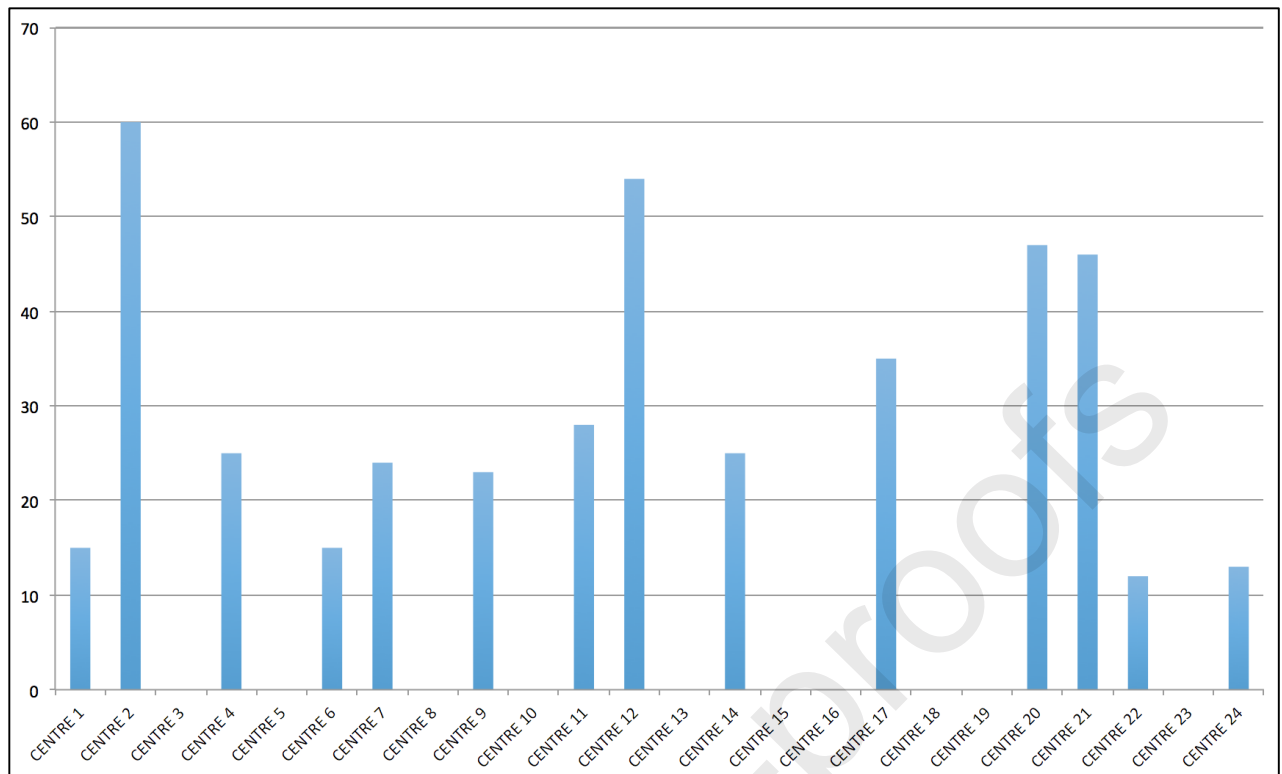


Figure 2: number of patients per center treated with a prostate seed implant in Belgium in 2018

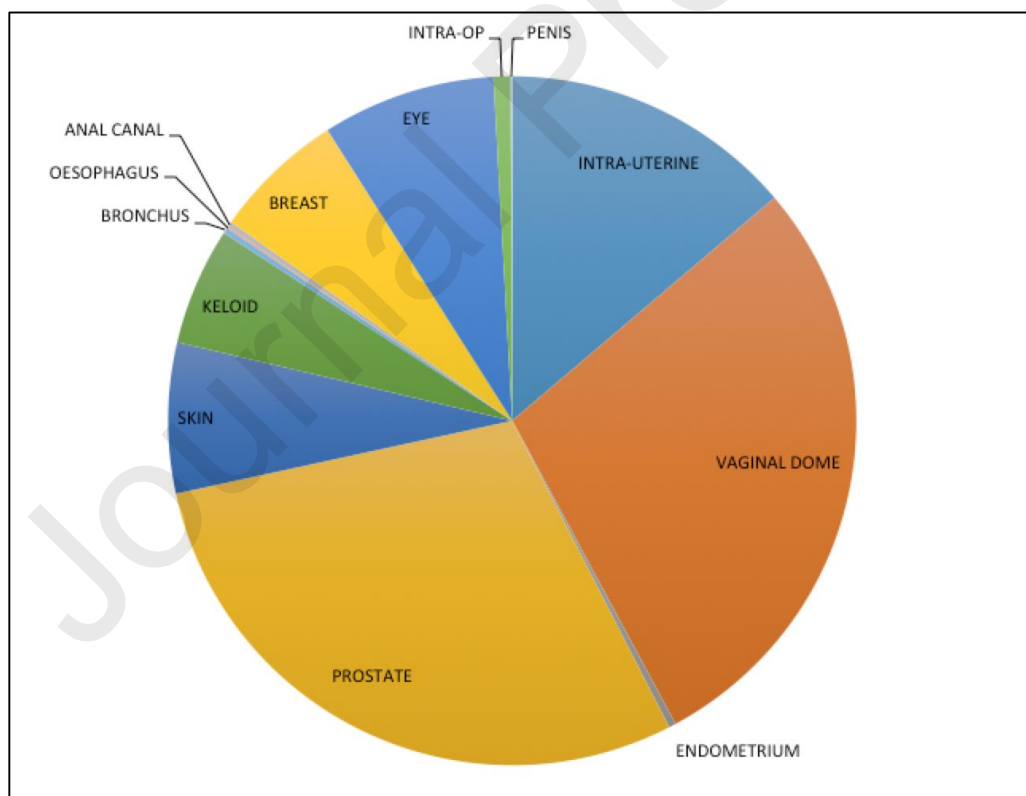


Figure 3: Distribution of the pathologies treated with brachytherapy in 2018

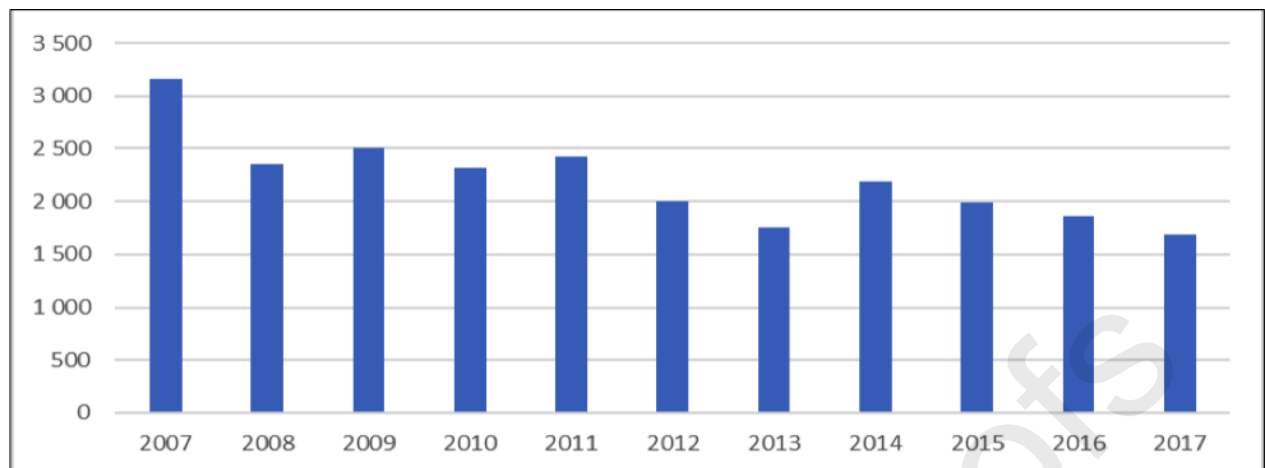


Table 1: Total number of BT-procedures performed in Belgium over the last ten years

Sites and number of HDR/PDR treatments	No. of patients	% of total afterloading- BT patients	Institutions	Average/Institution
Gyn. - vaginal vault	421	44,46%	15	28
Gyn. - intra-uterine	205	21,65%	14	15
Skin	105	11,09%	7	15
Keloid	82	8,66%	8	10
Breast	92	9,71%	2	46
Prostate HDR	15	1,58%	1	15
Intra-operative (Sarcoma)	12	1,27%	3	4
Gyn. - endometrial	5	0,53%	3	2
Lung - bronchus	4	0,42%	2	2
Anal canal	4	0,42%	4	1
Oesophagus	1	0,11%	1	1
Penis	1	0,11%	1	1

Table 2: Sites and numbers of HDR/PDR-BT procedures, distribution, number of institutions and average number per institution in 2018.

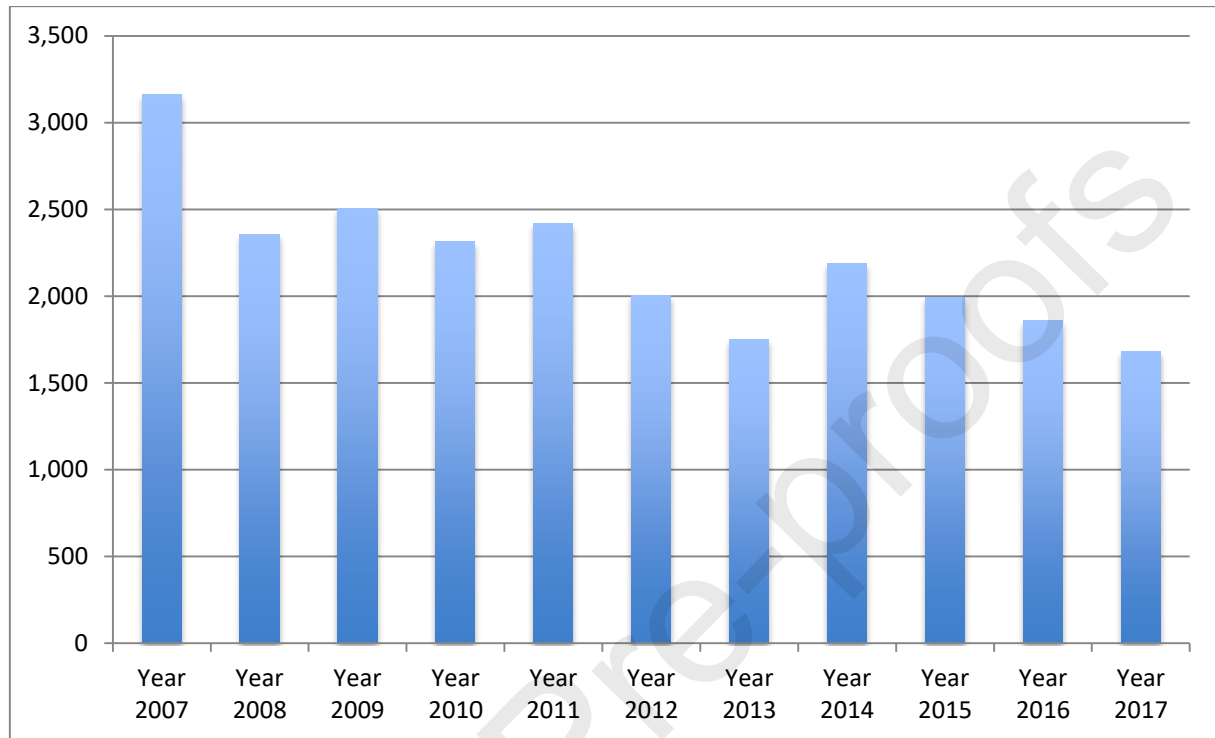


Table 1: Total number of BT-procedures performed in Belgium over the last years

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