Patterns of care study of brachytherapy in New South Wales: malignancies of the uterine corpus

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Abstract

Purpose: There are limited data at a population level on adjuvant brachytherapy (BT) practice for uterine corpus malignancies. The aims of the current study were to describe BT practice for this disease in New South Wales (NSW), to assess quality of BT, and to determine if a caseload effect on quality exists.

Material and methods: Patient, tumour, and treatment related data were collected from all nine NSW radiation oncology departments that treated patients with BT. Included patients had malignancy of the uterine corpus with treatment including BT. Brachytherapy quality was assessed using published quality benchmarks. Higher gynaecological BT caseload departments were compared with lower caseload departments.

Results: One hundred sixty-three NSW residents with gynaecological cancer were treated with BT. The four higher gynaecological BT caseload departments treated a median of 25.5 NSW residents (range 22-38), compared to median 10 (range 3-18) in the five lower caseload departments. Seventy-five patients underwent BT for uterine malignancies. Most patients had early stage endometrioid disease and were treated adjuvantly with intravaginal cylinders using high-dose-rate BT. Doses were in accordance with guideline recommendations in 83% of cases, and BT was appropriately indicated in 76% of cases. Higher caseload departments were more likely to treat with guideline doses (96% vs. 53%, \( p < 0.001 \)) but there was no difference in compliance rate with treatment indications (\( p = 0.75 \)).

Conclusions: Brachytherapy patients, techniques, and numbers/unit for uterine corpus malignancies were similar in NSW compared to the USA but more dispersed than in Western Europe. Doses prescribed may not be optimal in lower gynaecological BT caseload departments – the significance of this represents an area in which more research is needed.

Key words: brachytherapy, caseload volume, endometrial cancer, quality, patterns of care studies.

Purpose

Retrospective Patterns of Care Studies (POCS) seek to improve the quality of technical care by examining processes, structures and/or outcomes of care. The rationale is that differences exist in care; that these differences can be measured against explicit criteria and against each other; that deficiencies in care may affect outcome, and that these deficiencies, having been identified, are correctable, thereby improving patient outcome [1]. We performed the first comprehensive, population-based brachytherapy (BT) POCS in Australia. Collection of these data enabled an overview of actual New South Wales (NSW) BT use for comparison with our model of optimal BT utilization, showing that gynaecological BT is underutilized in NSW, reported previously [2]. The other aim of this POCS was to study patterns of practice of BT in NSW, with a particular focus on quality of care.

Herein, we focus on these results as they pertain to BT for uterine corpus malignancies.

Worldwide, gynaecological cancer in total is responsible for over 14% of female cancer deaths, more than that of breast cancer or female lung cancer. The international incidence of endometrial cancer in 2008 totalled 287,000, making it the 6th commonest female malignancy [3]. Brachytherapy is an integral part of endometrial cancer treatment [4,5], and the publication of the results of the PORTEC2 randomized trial, showing equivalence between adjuvant BT compared to pelvic external beam radiotherapy (EBRT) for intermediate risk endometrial cancer, is likely to further increase the utilization and importance of BT for this disease [6]. Despite this, current BT practice for uterine corpus malignancies is not well studied at a population level. There have been no POCS addressing endometrial cancer in Australia, and only
one survey of Australian gynaecological BT protocols, which provided limited data on how these patients are being treated with BT [7]. Similarly, there is very limited international literature detailing patterns of radiotherapy practice for uterine corpus malignancies [8-11].

The current study therefore had three aims, which were to: 1) describe the Patterns of Care of BT for malignancies of the uterine corpus in NSW; 2) assess the quality of BT in NSW for uterine corpus malignancies; and 3) determine whether there is a caseload effect on quality of BT for uterine corpus malignancies.

**Material and methods**

In 2005, a retrospective BT POCS was performed. The population for this manuscript was all NSW residents with a diagnosis of malignancy of the uterine corpus, treated with BT in NSW in 2003. Patients with cancer of the uterine cervix were excluded. New South Wales is the largest state of Australia, with a population of 6.6 million in 2003, 63% of whom lived in Sydney [12]. Site visits and data collection by the principal investigator were made to all nine radiation oncology departments in NSW that deliver BT. Collected data were entered into an Access database and then transferred into SPSS v15.0. Logic checks and descriptive analyses were performed to identify data errors and inconsistencies.

Quality of BT treatment was assessed using the published benchmarks, assessing concordance with NSW recommended doses and with treatment indications [4]. Adjuvant monotherapy doses recommended by the NSW guidelines were for low-dose-rate (LDR) BT 50-60 Gy, or for high-dose-rate (HDR) BT 30-40 Gy in 4-6 fractions. Doses were compared using the linear quadratic equation to convert HDR BT doses to equivalent LDR doses, which are approximately equivalent to standard fractionation at 2 Gy per fraction (EQD). For late effects, \( \alpha/\beta = 3 \), and for early effects and modelling of tumour control \( \alpha/\beta = 10 \) [13]. The HDR monotherapy doses recommended are thus EQD2 (\( \alpha/\beta = 10 \)) = 44-56 Gy. Combined modalities treatment doses recommended were 45-54 Gy EBRT in 1.8-2.0 Gy fractions with BT boost by LDR 20 Gy, or by HDR 15-18 Gy/2-4 fractions, EQD2 (\( \alpha/\beta = 10 \)) = 67-76 Gy. Prescribed doses were scored as appropriate if they fell within the range of these recommendations. Note that the NSW recommendations are similar to those of the American Brachytherapy Society but with a broader range [5]. Treatment with adjuvant BT was scored as potentially inappropriate if delivered to patients with stage I disease without adverse pathological features (stage IC, lymphovascular space invasion, grade 3, or close margins) giving an indication for adjuvant RT (BT with or without EBRT) [4]. Brachytherapy dose and treatment indication appropriateness was compared between higher and lower gynaecological BT caseload departments, defined as the four departments that performed more gynaecological BT compared to the five departments that performed fewer.

Categorical variables were compared using the chi-square test. The study was approved by all relevant Human Research Ethics Committees and carried out in accordance with the Helsinki Declaration. Patient and departmental data were de-identified.

**Results**

In NSW in 2003, there were 15 radiation oncology departments, of which 9 (60%) treated patients with BT, all administering gynaecological BT. After exclusion of 20 patients resident interstate, 163 NSW gynaecological cancer patients were treated with BT in 2003 (Table 1), most for cervical cancer (\( n = 76 \)) or uterine malignancies (\( n = 75 \)). The four higher gynaecological BT caseload departments treated 111 (68%) of the patients, median 25.5 per department (range 22-38). The five lower gynaecological BT caseload departments treated the remaining 52 (32%) patients, median 10 each (range 3-18). Mean age of patients with uterine malignancies was 65 (range 42-88) years. Patient stage and histology are shown in Table 2: 77% had early stage disease and 80% had non-papillary serous/clear cell adenocarcinomas.

**Table 1. Gynaecological brachytherapy activity, New South Wales cancer patients, 2003**

| Institution | Gynaecological primary tumour site | Total |
|-------------|-----------------------------------|-------|
|             | Vagina | Cervix | Uterus | Ovary | n   | (%) |
| 1           | 2      | 12     | 7      | 1     | 22  | 13  |
| 2           | –      | 3      | –      | –     | 3   | 2   |
| 3           | 2      | –      | 14     | –     | 21  | 1   | 38  | 23  |
| 4           | –      | 4      | 1      | –     | 5   | 3   |
| 5           | 1      | 8      | 9      | –     | 18  | 11  |
| 6           | 2      | 8      | 6      | –     | 16  | 10  |
| 7           | 1      | 15     | 10     | –     | 26  | 16  |
| 8           | 1      | 1      | 8      | –     | 10  | 6   |
| 9           | –      | 11     | 13     | 1     | 25  | 15  |
| Total       | 9      | 76     | 75     | 3     | 163 | 100 |
As shown in Table 2, five patients had recurrent uterine corpus malignancy treated with BT. Two were treated palliatively, and three underwent definitive combination EBRT and BT. Seventy patients had curative treatment, including BT for their initial disease presentation and are the subject of the remainder of the report in this section. Sixty-nine of these patients had adjuvant treatment post hysterectomy and one patient underwent neo-adjuvant BT.

Intra-vaginal cylinders with library plans were used by six departments to treat 64 (91%) of the 70 patients. One department used ovoids, treating 5 (7%) patients, and one department treated one patient only with tandem and ovoids neoadjuvantly. These two departments used orthogonal film based planning. Low-dose-rate caesium BT was used by two departments to treat 13 (19%) of the patients, pulsed-dose-rate (PDR) iridium was used by one department (treating as LDR) to treat 1 (1%) of the patients, and HDR iridium BT was used by five departments treating 56 (80%) of the patients.

Twelve patients were treated with adjuvant LDR BT monotherapy at two departments. All were dosed to the mucosal surface, and 10 of the 12 patients were dosed to 60 Gy (range 21-60 Gy). Adjuvant HDR BT monotherapy was used to treat 44 patients at five other departments. Four of these patients had dose prescribed to 0.5 cm below the vaginal mucosal surface: 15 Gy in 3# or 30 Gy in 6#. The other 40 patients were dosed to the mucosal surface (see Table 3), with median EQD2 being 44 Gy (range 24-67 Gy).

Thirteen of the 70 (19%) patients underwent adjuvant pelvic EBRT (in addition to BT) at five of the nine departments (Table 4). Median total EQD2 at the vaginal mucosal surface was 74 Gy (range 61-91 Gy).

As measured by conformity to guideline recommendations, doses were appropriate in 83% of patients.
Higher gynaecological BT caseload departments were more likely to treat to an appropriate dose (45 of 47 patients, 96%) than lower BT caseload departments (10 of 19 patients, 53%), $p < 0.001$. There were no significant differences by BT dose rate ($p = 0.33$).

Treatment with adjuvant BT was scored as potentially inappropriate if delivered to patients with stage I disease without adverse pathological features (stage IC, lymphovascular invasion, grade 3, or close margins) giving an indication for adjuvant RT (BT with or without EBRT) (5): 8 of 34 cases (24%), with no significant difference by gynaecological BT caseload ($p = 0.75$) – Fig. 2.

**Discussion**

The patients in this study were a population-based sample, and were similar to those in the SEER database, with 80% having adenocarcinomas of non-papillary serous/clear cell subtype, and 82% of these being stage I-II; compared to SEER: 90% of uterine malignancies being these non-high risk histological subtypes and 84% of these stage I-II [14]. Treatment in NSW was also similarly distributed to that in the USA, with 91% of NSW patients undergoing adjuvant BT being treated with an intra-vaginal cylinder, compared to the American Brachytherapy Society survey of adjuvant vaginal BT for endometrial cancer, also covering 2003 [8]: vaginal cylinders were used by 75% of respondents. In the two areas, a similarly low proportion of departments used LDR: 2 of 8 (25%) NSW departments compared with 31% of respondents in the ABS survey. LDR and HDR appear to be equally effective and safe, but the latter has well-recognized advantages in terms of patient convenience and comfort [15]. In our POCS, there was no difference between HDR and LDR prescriptions in terms of proportions of patients being treated to guideline recommended doses. There was, however, a large difference in the assessment of normal tissue doses: in the NSW POCS only the two departments using LDR BT, and ovoids recorded bladder and rectal doses in 8 of the 70 (11%) patients, compared to 78% of respondents for bladder and 80% for rectal doses in the ABS survey. The difference may be attributable to differences

![Fig. 1. Appropriateness of adjuvant radiotherapy dose, by departmental gynaecological brachytherapy caseload volume ($p < 0.001$). Appropriate dose was as recommended by New South Wales guidelines [5]](image1)

![Fig. 2. Appropriateness of adjuvant brachytherapy indication, by departmental gynaecological brachytherapy caseload volume - stage I endometrioid adenocarcinoma of the uterus ($p = 0.75$). Appropriateness of brachytherapy indication was as recommended by New South Wales guidelines [5]](image2)

### Table 4. Combination external beam radiotherapy and brachytherapy adjuvant dosing schedules

| Department | Pelvic EBRT dose fractions (Gy/#) | Brachytherapy dose rate | Brachytherapy dose and fractions (Gy/#)† | Total EQD2 at vaginal mucosal surface | Number of patients |
|------------|----------------------------------|-------------------------|------------------------------------------|--------------------------------------|-------------------|
| 5          | 45/25                            | HDR                     | 12/2                                      | 61                                   | 2                 |
|            | 50.4/28                           |                         |                                          | 66                                   | 1                 |
| 6          | 50.4/28                           | HDR                     | 26/3                                      | 91                                   | 1                 |
| 7          | 50.4/28                           | LDR                     | 20/1                                      | 70††                                  | 1                 |
| 8          | ?                                 | HDR                     | 24/4                                      | ?                                    | 1                 |
| 9          | 50.4/28                           | HDR                     | 18/3                                      | 74††                                  | 7                 |

EBRT – external beam radiotherapy, Gy – Gray, EQD2 – equivalent dose at 2 Gy/#, $\alpha/\beta = 10$ [14]. † – brachytherapy doses are normalised to vaginal mucosal surface, †† – total dose within guideline recommendations [5].
in guideline recommendations; the NSW guidelines make no recommendations regarding dose to normal tissue reporting [4]. The ABS does recommend doses to organ at risk reporting, although the ABS document does hedge the recommendation with the comment “...with the use of fixed geometry applicators, such as vaginal cylinders, localization radiographs need not be performed” [5]. Other reasons for the lack of normal tissue dose reporting in the HDR treated NSW POKS may be the reported low rate of rectal and urinary complications experienced by this group of patients [15].

There was a wide variation in adjuvant doses delivered in NSW, with 15 different total doses prescribed across the eight treating departments, with the EQD2 dose ($\alpha/\beta = 10$) ranging from 21 Gy to 91 Gy. This variation in dose may reflect the lack of published dose response data, but it is concerning that in most departments more than one dose had been prescribed. There may have been clinical reasons for individualization of doses in particular patients. The ABS survey also revealed a wide variation in dose prescriptions and fractionations [8]. Overall, when measured against the recommendations of the NSW guidelines [4], dose prescriptions were within the recommended range in 83% of patients. Higher gynaecological BT caseload departments were significantly more likely to treat to a recommended dose than lower caseload departments (96% vs. 53% of cases, $p < 0.001$).

It is recognized that the NSW POCS assessed treatment for 2003 but the NSW guidelines were not published until 2004. Nevertheless, these guidelines were widely distributed in NSW in various drafts for some ten years prior to publication and provide a reasonable summation of what was considered benchmark treatment for gynaecological malignancies in NSW in the early 2000s. A further explanation may be that the NSW guidelines simply reflect the practice of the larger gynaecological departments, and hence the greater likelihood of the higher gynaecological BT caseload departments treating according to these guidelines. When assessing the appropriateness of adjuvant BT indication for stage I patients in comparison to the NSW guidelines, there was no significant difference between departments by caseload, with treatment being appropriate in 76% of cases overall (Fig. 2). This is higher than that determined by applying the same criteria to a recent SEER study, in which the use of adjuvant BT (with or without EBRT) was appropriate in only 60% of treated stage I patients. Although, some of the patients potentially inappropriately treated in that study may have had other relative indications not recorded in the manuscript, such as lymphovascular invasion [10].

Whilst there are data correlating outcome with caseload in treating cervical cancer [16-18], and there have been two reports showing potential benefits from sub-speciality surgical training on outcome in uterine malignancies [19,20], this is the first report assessing the effect of radiotherapy provider caseload on treatment for this disease. Gynaecological BT, specifically BT for uterine malignancies, is generally more dispersed in NSW and the USA compared to Western Europe, with fewer cases treated per centre (Table 5). Although this is potentially a factor that may adversely impact on the quality of cervical BT and outcomes [16-18], it may not be an important issue in the treatment quality of uterine cancers. A further

| Tumour site       | Cases/Centre/Year | NSW 2003          | ABS, 1992 [21] | UK, 2004 [22] | Italy, 2002 [23] | Spain, 2002 [23] |
|-------------------|-------------------|-------------------|----------------|----------------|------------------|------------------|
|                   | All               | Higher caseload | Lower caseload |                |                  |                  |
| All               | Mean              | 18                | 27.8           | 10.4           | 61               | 35               | 76               |
|                   | Median            | 18                | 25.5           | 10             | –                | –                | –                |
|                   | Range             | 3-38              | 22-38          | 3-18           | 13-174           | 21-48 (95% CI)   | 54-99 (95% CI)   |
|                   | > 25 cases        | 22%               | 50%            | 0%             | 88%              | –                | –                |
| Uterine cervix    | Mean              | 8.4               | 13.0           | 4.8            | –                | –                | –                |
|                   | Median            | 8                 | 13             | 4              | 19               | –                | –                |
|                   | Range             | 1-15              | 11-15          | 1-8            | 9-45             | –                | –                |
|                   | > 10 cases        | 44%               | 100%           | 0%             | 37%              | –                | –                |
| Uterine corpus    | Mean              | 9.4               | 12.8           | 4.8            | –                | –                | –                |
|                   | Median            | 8.5               | 11.5           | 6              | –                | –                | –                |
|                   | Range             | 0-21              | 7-21           | 0-9            | –                | –                | –                |
|                   | > 10 cases        | 25%               | 50%            | 0%             | 28%              | –                | –                |

NSW – New South Wales, ABS – American Brachytherapy Society, UK – United Kingdom, 95% CI – 95% confidence interval, “–” – not available
consideration is that actual gynaecological BT utilization is close to our previously modelled optimal rate in the UK and Spain (where gynaecological BT is concentrated), but sub-optimal in Italy (also concentrated) and in NSW and SEER (dispersed). The significance of concentration or dispersal of uterine BT per centre and whether this may impact on utilization of BT is unknown [2].

It should be noted that almost all patients in this study underwent adjuvant vaginal vault BT, with only three patients having definitive treatment. Definitive BT with BT for endometrial cancer is used rarely, but can often be curative [24]. This study did have a number of limitations. It was retrospective, involved small patient numbers, represents state-of-play in 2003, and therefore not necessarily reflecting current NSW practice. However, although there have been dramatic changes in cervical brachytherapy with widespread incorporation of MRI assisted 3D planning, we contend that there have been minimal changes in vaginal vault brachytherapy for endometrial cancer. This is likely secondary to the good results achieved with vault brachytherapy for this disease in terms of high rates of local control and minimal radiation related morbidity. Nevertheless, there is a paucity of Patterns of Care data, either of current or of recent practise, to confirm this. Robust vaginal vault BT treatment quality indicators against which performance can be measured are lacking. Importantly, this study reports technical factors but not outcome data. These are areas in which future research is likely to be beneficial.

The study has a number of strengths. Although numerous studies have found a correlation between provider caseload for prostate and cervical BT quality and/ or outcomes, none have assessed whether this caseload effect exists for BT in the context of uterine corpus malignancies. This is the first paper to do so. It adds to the sparse population level data on brachytherapy use in this disease. It is the final in a series of three publications summarising brachytherapy Patterns of Care in New South Wales, and completes the picture with the other two publications also assessing patterns of care for brachytherapy and caseload effects on quality for cervical [18] and prostate cancer [25].

Conclusions

In the case of BT for uterine corpus malignancies, tumour types and BT techniques in NSW in 2003 were similar to those in the USA. A wide range of adjuvant vaginal vault doses were delivered, although usually within the recommended range. New South Wales gynaecological BT (like that of the USA but not Italy, Spain or the UK) was dispersed amongst a large number of treating departments, although the significance of this is not clear: higher gynaecological caseload departments were more likely than lower caseload departments to treat to recommended doses (in the absence of published dose response data), but were equally likely to treat patients with guideline recommended indications. Further research as to treatment quality indicators for BT in this disease is needed.

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Meeting Presentations

This manuscript is based on data presented at the following Scientific Meetings: 1. The Royal Australian and New Zealand College of Radiologists 56th Annual Scientific Meeting, Sydney, October 2005, and 2. The Royal Australian and New Zealand College of Radiologists 61st Annual Scientific Meeting, Perth, October 2010 [26].

Disclosure

Authors report no conflict of interest.

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