More innovative approaches to radiotherapy are key to enhancing the treatment options available to cancer patients, providing a more patient-centred approach. By using the latest computerised planning and imaging techniques, brachytherapy offers high precision, targeted radiotherapy, providing good efficacy and tolerability outcomes, coupled with short treatment times.

Brachytherapy was first used to treat cancer over 100 years ago. Both external beam radiation therapy (EBRT) and brachytherapy techniques have been refined over the past 30 years as advances in imaging and computing technology have been incorporated into the planning and treatment process. Other recent external radiotherapy techniques, such as intensity modulated radiation therapy (IMRT), stereotactic radio-surgery (SRS) and proton beam therapy, have also been developed although these treatments involve a higher installation and delivery cost and are generally not widely available.

Brachytherapy: High precision, targeted radiotherapy

Unlike EBRT which delivers an external radiation source through healthy tissue ('from the outside, in'), brachytherapy delivers the radioactive dose directly within or adjacent to the tumour ('from the inside, out'). Computer-controlled remote robotic afterloading devices position a small radioactive source, with a limited field of radioactivity, within specially designed applicators, to deliver a high precision dose to the target area. This allows a tailored radiation dose to be precisely delivered to the target area while minimising unwanted exposure to the surrounding healthy tissues and organs, so-called 'conformal radiotherapy'. Furthermore, the very nature of the physics of brachytherapy helps minimise exposure to healthy tissues. Brachytherapy depends on the 'inverse square law', which states that around a source of radiation the dose 'falls-off' at the square of the distance. Thus, the tissues around the treated tumour receive a much lower dose than anticipated by other radiation methods.

The concept of dose escalation, i.e. increasing the radiation dose in order to maximise the biological and clinical effect in tackling tumours, is an important goal of all forms of radiotherapy. However, it has been an important challenge to successfully increase the dose, but not at the expense of damage to healthy tissues and thus toxicity. The essential nature of delivering radiation 'from the inside, out', allows dose escalation to be achieved with brachytherapy, either as monotherapy or in combination with EBRT. The fundamental features of brachytherapy translate into tangible benefits for patients and healthcare services. Brachytherapy can result in shorter treatment times, minimising disruption to patients and allowing a faster return to everyday life. In addition, treatment is well-tolerated and helps to preserve quality of life, together with the potential to realise lower utilisation of healthcare resources and associated costs. There is a high degree of dosing flexibility, providing a greater opportunity to personalise treatment, and also the overall length of the treatment programme is shortened from weeks to days in many instances, reducing disruption to patients' lives.

The ability of brachytherapy to deliver high radiation doses over a short time period is important for treatment efficacy as both the total radiation dose and the rate at which it is delivered effect cancer cell killing. More cancerous cells are destroyed when a treatment dose is administered over a short time frame and, although High Dose Rate (HDR) brachytherapy achieves a similar overall killing effect as Low Dose Rate (LDR) brachytherapy or EBRT, it does so at a significantly lower total dose. A shorter course of therapy may also offer better tumour control as cells have a decreased opportunity to repopulate between treatments. Rapid dose decline of the radioactive source increases with distance from the tumour site and results in decreased toxicity to healthy surrounding tissues. In addition, short treatment times with brachytherapy can help ensure that the total dose is delivered, whereas with prolonged treatment, such as with standard EBRT, the risk of non-adherence to the treatment plan is increased.

Brachytherapy efficacy and safety outcomes:

Patient benefits

Brachytherapy is an efficacious treatment option that is used worldwide to treat a wide range of cancers and other diseases (Figure 1). It is the standard treatment for cervical cancer and is widely used in prostate cancer. It is also used in a wide range of other cancers including breast, skin, anal and rectal, and head and neck cancers. A number of organisations, including the American Brachytherapy Society (ABS), the American Society of Radiation Oncology (ASTRO), the European Society of Therapeutic Radiology and Oncology (ESTRO) and the National Comprehensive Cancer Network (NCCN) support the use of brachytherapy in their treatment guidelines. In addition, thousands of published papers provide significant efficacy and safety evidence.

## Brachytherapy in gynaecological cancer

Brachytherapy has long been a standard of care for gynaecological cancers. Today, innovative technologies like adaptive, image-guided brachytherapy are setting new benchmarks for treatment. A ‘patterns of care’ study in the United States showed that over 90 per cent of cervical cancer patients were treated with EBRT plus brachytherapy. Brachytherapy is typically used in combination with surgery, but is also an option for inoperable disease. In endometrial cancer, brachytherapy is typically used in combination with surgery, but is also an option for inoperable disease, while it is a standard treatment option for vaginal cancer, often in combination with EBRT for more advanced disease.

Key benefits in gynaecological cancer include comparable efficacy (both LDR and HDR brachytherapy show similar efficacy to surgery; decreased toxicity to the rectum and bladder) patient convenience (HDR brachytherapy can be delivered on an outpatient basis, reducing treatment times, which means better patient acceptability and lower healthcare costs).

### Gynaecological cancer: Efficacy

Both LDR and HDR brachytherapy achieve similar recurrence rates to surgery for early stage cervical cancer, offering patients a real alternative to hysterectomy. They offer an
equally effective alternative to surgery (hysterectomy) in early stage cervical cancer (stages IA2 and IB1) and are the standard treatment for bulky (stage IB2) or locally advanced disease (stages IIA-IVA), typically in combination with EBRT and chemotherapy. Both LDR and HDR intracavitary brachytherapy are used to treat cervical cancer. A recent meta-analysis comparing HDR and LDR brachytherapy showed no significant difference in overall mortality between the two approaches (HDR, 35.1%; LDR 34.1%; odds ratio 0.96) over a median follow-up of five years. Mortality rates did not differ between treatments for the subgroups of patients with stage I, II or III disease and local recurrence was similar between the treatments. Variations in outcomes between LDR and HDR brachytherapy in stage III patients have been reported, suggesting that LDR brachytherapy may be preferable for large, bulky tumors.

**Brachytherapy in prostate cancer**

Recent advances in brachytherapy have made it an accurate and practical treatment option for patients with low-, intermediate- and high-risk disease. Both LDR brachytherapy (permanent seeded implantation) and HDR brachytherapy are used to treat prostate cancer. Key benefits in prostate cancer include equivalent efficacy (cancer control rates) compared with EBRT and surgery as well as significantly shorter treatment times compared with EBRT (day(s) compared with weeks), which means better patient acceptance. It allows effective dose escalation while minimizing toxicity and there is a lower incidence of urinary and sexual function adverse events compared with surgery and a low incidence of bowel adverse events compared with EBRT. It is also more cost-effective than other forms of radiotherapy.

**Prostate cancer: Efficacy**

Five-year survival rates demonstrate brachytherapy is as effective as EBRT or surgery for prostate cancer.

**Prostate cancer: Efficacy, LDR brachytherapy**

Brachytherapy has demonstrated equivalent efficacy to radical prostatectomy and to EBRT in patients with prostate cancer, even in patients with larger tumour size (T1-T2c) and without long catheters for the source are implanted, allowing the treatment of more advanced disease. Brachytherapy allows for accurate dosing as the clinical target volume is determined after the catheters for the source are implanted and organ motion is prevented, reducing the need for additional safety margins. Furthermore, radiation can be placed in extra-prostatic tissue, allowing for the treatment of more advanced disease. Freedom from bRFS of 89-100% has been reported for HDR brachytherapy alone in low- and intermediate-risk patients, which compares favourably with those seen for permanent LDR implants, although follow-up durations to date have been shorter than in LDR studies.

**Prostate cancer: Efficacy, HDR brachytherapy**

In recent years, HDR brachytherapy has been developed as a treatment for intermediate- to high-risk prostate cancer. HDR brachytherapy uses temporary implantation of a 192Ir source to deliver the radiation dose to the target treatment area (figure 2). HDR brachytherapy allows for accurate dosing as the clinical target volume is determined after the catheters for the source are implanted and organ motion is prevented, reducing the need for additional safety margins. Furthermore, radiation can be placed in extra-prostatic tissue, allowing for the treatment of more advanced disease. Freedom from bRFS of 89-100% has been reported for HDR brachytherapy alone in low- and intermediate-risk patients, which compares favourably with those seen for permanent LDR implants, although follow-up durations to date have been shorter than in LDR studies.

**References**


**FIGURE 2**

Shows 3D imaging and dose distribution with treatment needles in situ.