

BRACHYTHERAPY IN HORSES

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DAVID DONALDSON BVSc(Hons), DipECVO, MRCVS considers the use of low-dose rate and high-dose rate brachytherapy, especially development of computerised planning to allow more precise delivery.

ALTHOUGH the diagnosis of neoplasia is relatively uncommon in horses, the periorcular region is commonly involved, with sarcoïd and squamous cell carcinoma being the most common diagnoses.

Management is commonly multimodal and integrates combinations of surgery, chemotherapy, immunotherapy, cryosurgery and radiation therapy (RT).

Surgical debulking is commonly performed and improves the success rate of adjunctive therapies such as RT. Attempts at complete surgical excision followed by reconstructive blepharoplasty procedures are limited in horses due to the need to preserve a functional eyelid and the lack of skin that can be mobilised around the eye. The equine skin is firmly attached to the underlying connective tissue and has poor superficial blood supply, and, therefore, the mobilisation of adequate skin to be used in blepharoplasty procedures is limited (Gilger and Stoppini, 2005).

Brachytherapy involving various radionuclides has been described in horses and, given the limitations of surgical interventions, represents an important adjunctive treatment for cases of periorcular neoplasia.

Brachytherapy is a form of RT where the radiation source is in direct contact with the patient. The two main types of brachytherapy are interstitial, in which the radioactive implant is placed directly

inside the tumour volume, and contact or plesiotherapy, where the source is placed close to the tumour.

Contact brachytherapy may be further divided into intracavitary (such as nasopharynx), intraluminal (such as cervix), endovascular and surface (for example, skin) methods. Due to the rapid fall-off in dose around radioactive sources, brachytherapy is characterised by strong dose gradients, with the highest levels of radiation being evident near the source. This allows high doses of radiation to be delivered to a tumour (greater local tumour control) while minimising the exposure of surrounding normal tissue (fewer side effects).

In contrast to external beam RT in which deep-seated tumours can be irradiated, brachytherapy requires the placement of catheters directly into the tumour. Given this, brachytherapy is particularly suited to accessible tumours with well-defined margins.

Brachytherapy with radium (Ra-226) was first used in 1901, soon after the discovery of radium and its radioactivity. The dangers of radiation exposure were not appreciated in the early 1900s and, as a result, radium, with its mysterious properties such as luminescence when mixed with phosphor, led to its use in many consumer products such as the very popular glow in the dark watch and clock faces. Radium remained the isotope of choice for brachytherapy until the 1950s to 1960s, when it was replaced by reactor-based radionuclides such as cobalt-60, caesium-137, iridium-192, gold-198 and iodine-125. These “radium substitutes” have a long history of use in low-dose rate (LDR) brachytherapy implants for treatment of human head and neck, gynaecological, breast and prostate cancers. The radiation dose used in LDR brachytherapy is less than two gray (Gy)/hr (typically 40cGy/hr to 80cGy/hr).

The radioactive sources are usually coated in platinum or stainless steel and supplied in many forms, including wires, needles, tubes, pellets or seeds. Some examples of LDR brachytherapy treatments in people include permanent implantation of iodine-125 or gold-198 seeds for prostate cancer, and temporary implants of iridium-192 or caesium-137 for oropharyngeal and cervical cancer.

In horses, LDR brachytherapy has been successfully used to treat periocular sarcoid with a 98 per cent success rate at more than three years (Knottenbelt and Kelly, 2000), and is considered by some to be the “gold standard” for tumours of this nature at this site (Byam-Cook et al, 2006; Knottenbelt and Kelly, 2000).

In human radiation oncology the radiation safety concerns related to the manual handling of radiation sources have resulted in a decline in the use of LDR brachytherapy in favour of high-dose rate (HDR) brachytherapy (more than 12Gy/hr). In HDR brachytherapy a remote afterloading technique is used in which catheters are pre-placed in the tissue to be treated and the radioactive source is later loaded into these catheters by a computer-controlled delivery system after the patient is isolated in an appropriately shielded treatment room. This provides complete radiation

protection to the medical personnel delivering the treatment.

Modern HDR brachytherapy is possible due to availability of high specific activity Iridium-192 sources and developments in computer-controlled afterloading technology in the 1980s and 1990s. Similar concerns regarding radiation exposure exist for LDR brachytherapy in veterinary medicine and, as a result, LDR interstitial brachytherapy in horses is not permitted in some states and facilities in the US. In the UK, interstitial LDR brachytherapy is still used in a few facilities. The Animal Health Trust (AHT) is commissioning the Varian GammaMedplus iX afterloader ([Figure 1](#)), which will allow HDR brachytherapy to be performed in veterinary patients. HDR brachytherapy will be performed in the radiation protection bunker of The Kennel Club Cancer Centre recently opened at the AHT. Equine stocks have been incorporated into the bunker so HDR brachytherapy can also be performed in horses under sedation.

Cross-sectional imaging

The most recent development in the field of brachytherapy has been the integration of cross-sectional imaging into 3D treatment planning. Sophisticated, 3D cross-sectional image-based treatment planning utilising ultrasound, CT or MRI became established as a standard practice for human external beam radiation therapy in the 1980s and 1990s.

Such computerised planning is now being used in HDR brachytherapy and allows more precise delivery of the radiation dose. The afterloader uses brachytherapy treatment planning software showing the exact location of the pre-placed treatment delivery catheters. It may provide cross-sectional images for 3D reconstruction or 2D radiographic film. Using various contouring tools the gross tumour volume (GTV) is delineated ([Figure 2](#)). The GTV represents the tumour, which can be grossly visualised, palpated or seen using imaging.

The region to be treated is referred to as the planning target volume (PTV; [Figure 2](#)), which encloses the GTV with a margin (usually 5mm to 10mm in brachytherapy) to account for set-up errors, as well as physiological motion and fluctuations in the size and shape of organs. The contouring tools are also used to define adjacent normal structures and organs at risk (OAR; [Figure 2](#)). The OARs are those more sensitive to radiation and, in the case of periocular tumours, this includes the lens, cornea, lacrimal gland, retina and optic nerve.

The location of the treatment catheters is then incorporated into the treatment plan so the treatment may be simulated ([Figure 3](#)). The isodose lines, which show the distribution of the radiation dose around the source, are calculated by the treatment planning software and this may be viewed either in 2D or 3D ([Figure 3](#)). After the computer completes the initial calculations, the clinician (dosimetrist) can customise the radiation doses to conform to the target volume (PTV) while minimising the doses to the nearby normal tissues (particularly the OARs).

Once the treatment plan has been approved by the physician, the computer transfers the treatment

plan instructions to the afterloader. The programmed instructions tell the afterloader where to direct the radioactive source, which is on the end of a guide wire, and how long it will stay (dwell time) in each position (dwell positions). The resultant distribution of radiation is shown by the isodose lines ([Figure 3](#)).

For equine HDR interstitial brachytherapy at the AHT the horse will be sedated and placed in stocks in the radiation bunker. The treatment catheters, which have been pre-placed through the tumour, are then connected to the HDR afterloader. All staff leave the bunker and the horse is continually monitored through closed circuit TV monitors. The treatment takes five to 10 minutes depending on the size and complexity of the implant and the activity of the source. At the end of treatment the radiation source is retracted back into the HDR afterloader.

Due to financial constraints it is not feasible to perform advanced imaging such as CT on all horses with periocular neoplasms. A study is under way to compare the accuracy of using 2D radiographic film against 3D planning. This will potentially provide information to improve the efficacy of treatment using 2D planning. Other applications of HDR brachytherapy include equine skin tumours at non-periocular locations and a spectrum of neoplastic conditions in small animals, including injection site sarcomas in cats, anal gland adenocarcinomas in dogs, and nasal tumours in dogs and cats.

References

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Figure 1. The Varian GammaMedplus iX afterloader (HDR brachytherapy) in the radiation protection bunker of The Kennel Club Cancer Centre at the Animal Health Trust.

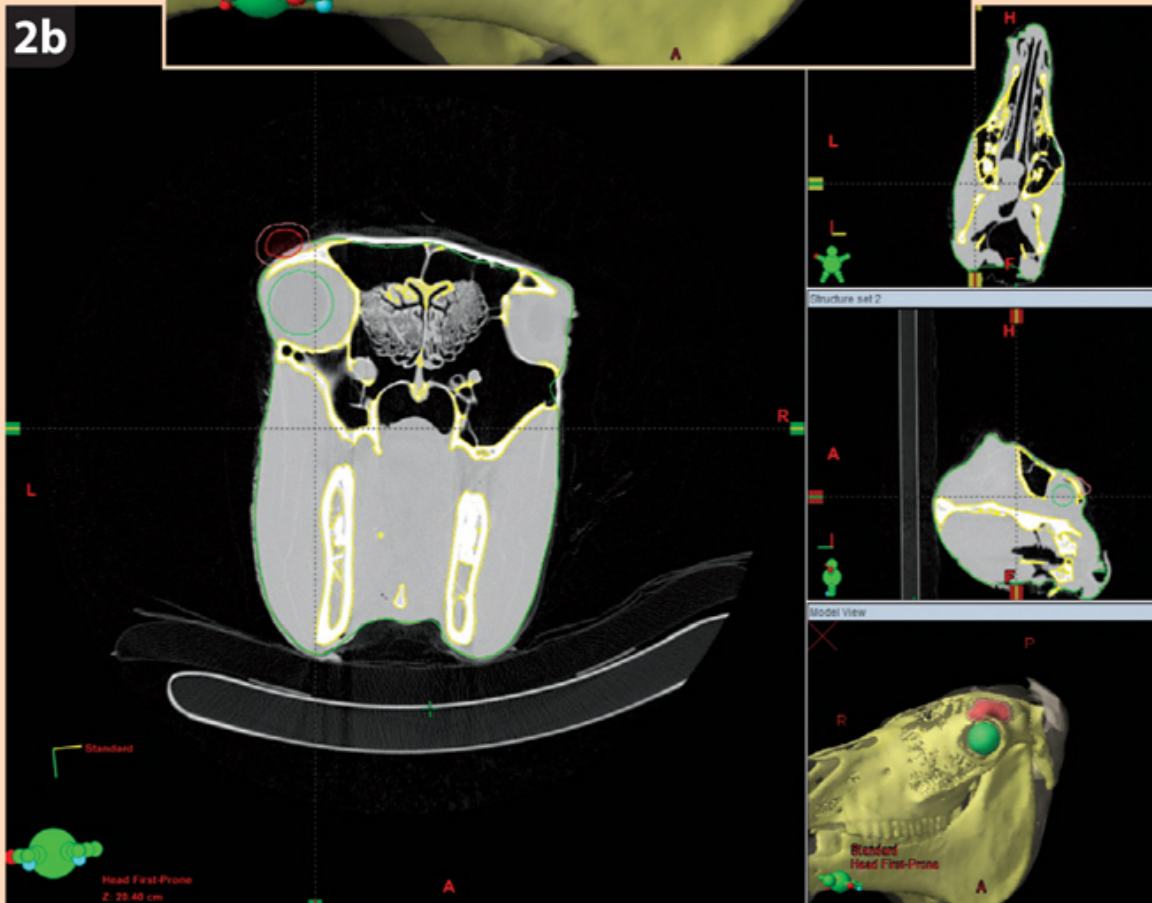


Figure 2a. A 3D colour-enhanced reconstruction. **Figure 2b.** A reconstructed 2D transverse slice reconstruction of a horse skull in the brachytherapy treatment planning software. Using various contouring tools, the gross tumour volume (GTV) is delineated in red and the planning target volume (PTV) is shown to surround the GTV in a translucent pink. The GTV represents the tumour, which can be grossly visualised, palpated or seen using imaging, while the region to be treated encloses the GTV with a margin (usually 5mm to 10mm in brachytherapy) to account for set-up errors as well as physiological motion and fluctuations in the size and shape of organs. The bone is shown in yellow, while the eye, which is labelled as an organ at risk (OAR) due to its increased sensitivity to radiation, has been highlighted in green.

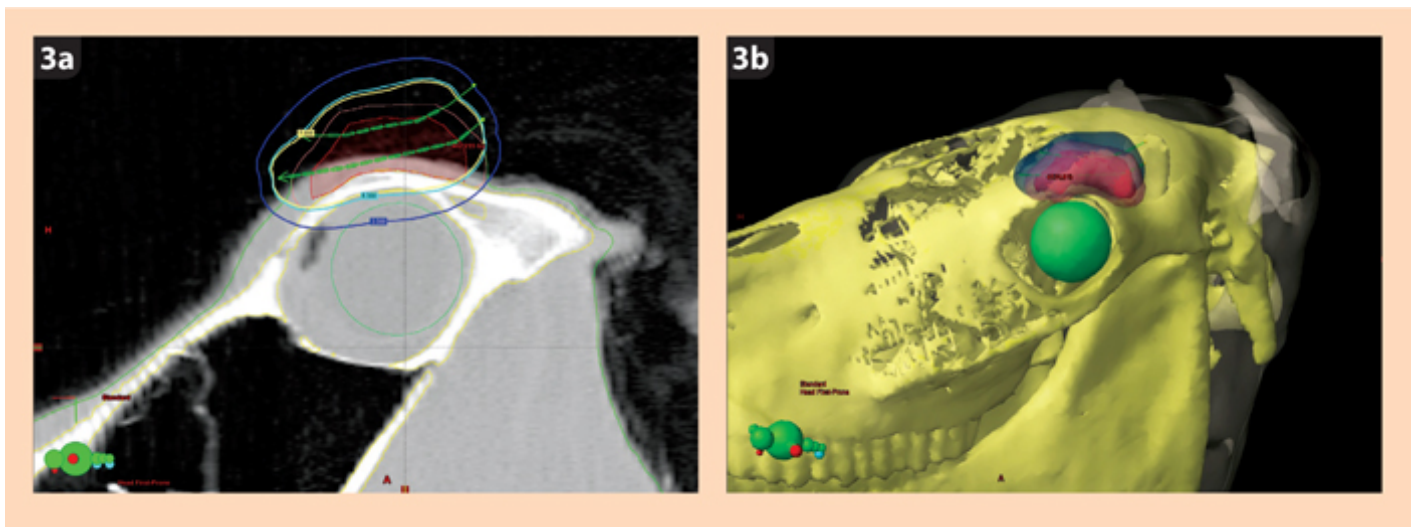


Figure 3. The locations of the treatment catheters are entered into the planning software, which allows the treatment to be planned and simulated. **3a.** 2D sagittal reconstruction shows the two

treatment catheters placed through the tumour, in green. The GTV is shown in red, the surrounding PTV in pink and the eye (an OAR) in green. The PTV is surrounded by isodose lines, which show the periphery of the regions receiving 7Gy (yellow), 6.3Gy (light blue) and 3.5Gy (dark blue). The treatment catheters are shown to have distended segments that correspond to the dwell points at which the radioactive source will stop (dwell times). The radioactive source, which is on the end of a guide wire, will be pushed out along each catheter and stop at each dwell point for the dwell time determined by the software. The resultant distribution of radiation is shown by the isodose lines.

3b. 3D reconstruction shows the two treatment catheters (green), GTV (red), PTV (pink) and the eye (green). Only one isodose is shown (90 per cent isodose) in translucent blue. The dose may be displayed either in grays (Gy) or a percentage of the dose delivered with respect to a reference point. In this case the 90 per cent isodose is the same as the 6.3Gy isodose line. The 3D images can be rotated and viewed in any plane and provide a means of rapidly reviewing the distribution of radiation doses to the GTV, PTV and OARs.