

# The Oncentra Prostate v4.x for ultrasound-guided real-time HDR brachytherapy in men with localised prostate cancer

Medtech innovation briefing

Published: 16 December 2014

[www.nice.org.uk/guidance/mib16](http://www.nice.org.uk/guidance/mib16)

## Summary

<b>Product summary and likely place in therapy</b> <ul style="list-style-type: none"><li>• The Oncentra Prostate is a real-time ultrasound-guided brachytherapy system designed to treat prostate cancer.</li><li>• The Oncentra Prostate would be used to manage intermediate- and high-risk localised prostate cancer where radiotherapy is indicated.</li></ul>	<b>Effectiveness and safety</b> <ul style="list-style-type: none"><li>• Three small feasibility studies (n=9, 15 and 20) confirmed the system's ability to provide the prescribed radiation dose to the prostate while keeping the dose to the surrounding organs at risk low.</li><li>• One cohort study (n=95) found the prevalence and severity of patient-reported side effects to be in the acceptable range, but no statistically significant associations between patient or dosimetric parameters and patient-reported outcomes.</li></ul>
<b>Technical factors</b> <ul style="list-style-type: none"><li>• The Oncentra Prostate provides 3D ultrasound visualisation of the prostate and enables insertion of brachytherapy applicators, treatment planning and treatment delivery in a single session.</li><li>• The Oncentra Prostate is only for use by clinicians trained and experienced in brachytherapy techniques.</li></ul>	<b>Cost and resource use</b> <ul style="list-style-type: none"><li>• Upgrading to the Oncentra Prostate 4 x from its predecessor system, the Oncentra Prostate 3 x, costs £34,250 per unit (excluding VAT). The cost for a new Oncentra Prostate 4 x (that is, not an upgrade) is estimated as £127,657 (excluding VAT).</li><li>• No evidence on cost and resource use was available.</li></ul>

## Introduction

Prostate cancer is the most common cancer and second most common cause of cancer death in men in the UK. Based on 2011 UK statistics, 110 men are diagnosed with and 30 men die from prostate cancer every day (Cancer Research UK, 2014a).

Men with prostate cancer develop both general and specific disease symptoms including

tiredness, weight loss, anorexia, difficulty and pain in passing urine, blood in the urine and bone pain (in cases of advanced metastatic disease).

A diagnosis of prostate cancer is established through a range of tests. These include: digital rectal examination; blood tests for the biomarker prostate-specific antigen (PSA); imaging tests such as MRI, computed tomography (CT) or ultrasound; and prostate biopsy. Based on the results of these tests, men with prostate cancer are categorised into 1 of 3 risk groups as outlined in NICE's guideline on [prostate cancer: diagnosis and treatment](#). These are:

- Low risk: PSA score of less than 10 ng/ml, and small size tumour confined within the prostate (T1–T2a), and biopsy result showing a Gleason score of less than 6.
- Intermediate risk: PSA score of 10–20 ng/ml, or tumour confined to the prostate involving more than 50% of 1 lobe (T2b), or biopsy results showing a Gleason score of 7.
- High risk: PSA score of more than 20 ng/ml, or tumour confined to the prostate involving both lobes (T2c and above), or biopsy results showing a Gleason score of 8–10.

Depending on their risk group, men with prostate cancer have the following treatment options:

- Active surveillance, which is where no treatment is had but men visit the hospital regularly for an examination and PSA test.
- Radical prostatectomy with or without removal of lymph nodes.
- External beam radiotherapy with or without brachytherapy.
- Monotherapy using brachytherapy.

For more information regarding these treatment options, see NICE's guideline on [prostate cancer: diagnosis and treatment](#).

NICE currently recommends 2 forms of radiotherapy as treatment options for prostate cancer. External beam radiotherapy (EBRT) involves using high-energy x-rays produced by an external radiation source (linear accelerator) to destroy the cancer cells. People having this treatment must attend hospital 5 days a week for several weeks. The second form is brachytherapy, whereby radioactive material is inserted directly into the prostate gland to

kill the rapidly dividing cancer cells. The radioactive material can be inserted permanently using radioactive seed implants, or temporarily by attaching the radioactive source to the end of a wire that is inserted for a short time. Men having this treatment need to attend hospital for their treatment once or twice. Brachytherapy can be used on its own or in combination with EBRT (sometimes called a 'boost dose'). High-dose-rate (HDR) brachytherapy is where a high-activity radioactive source (such as iridium-192) is temporarily inserted into the prostate to deliver a high radiation dose.

The clinician performing brachytherapy uses imaging technology to guide the insertion of the radioactive source into the prostate and to develop the radiotherapy treatment plan. For prostate brachytherapy the clinical team can image this process using CT, MRI or ultrasound.

HDR brachytherapy is usually performed with the patient under general anaesthetic, or with local anaesthetic and sedation (see NICE's interventional procedure guidance on [high dose rate brachytherapy in combination with external-beam radiotherapy for localised prostate cancer](#)). On average 16 thin plastic or metallic needles, called applicators, are inserted through the perineal skin behind the scrotum into the prostate gland (the number of applicators varies according to the size and shape of the prostate). A radioactive source is then inserted from the afterloading platforms into each applicator. The radiation dose is controlled by varying the time that the radioactive source spends at different positions within each applicator in the prostate (this will usually last a few minutes depending on the prescribed radiation dose), and this limits the radiation dose to the surrounding healthy tissues and organs. After the appropriate dose has been administered, the applicators are removed, leaving no radioactive material in the prostate gland.

Conventional prostate brachytherapy is administered in a 2-step approach, where the applicators are inserted while the patient is in the operating room, and the patient is then transferred from surgery to have a CT or MRI scan, or both. The clinician will use the images from the scan to define the radiation dose and to finalise the treatment plan, and then the radioactive sources are inserted into the applicators.

In contrast, the workflow for real-time HDR prostate brachytherapy is a single-step approach that allows the treatment to be provided in the operating theatre in a single session, without moving the patient. This is claimed to potentially reduce the procedural time and the risk that the applicators could become dislodged (Batchelar et al. 2011, Milickovic et al. 2001).

# Technology overview

This briefing describes the regulated use of the technology for the indication specified, in the setting described, and with any other specific equipment referred to. It is the responsibility of healthcare professionals to check the regulatory status of any intended use of the technology in other indications and settings.

## About the technology

### CE marking

Oncentra Prostate received a CE mark in May 1998. This was reissued in June 2013 and is valid until July 2017. The CE mark is held by the manufacturer, Nucletron, which is part of Elekta AB.

The individual components of the Oncentra Prostate system for HDR brachytherapy are listed below, alongside their device class:

- software (class IIb)
- afterloaders (class IIb)
- applicators (class IIa and IIb)
- radioactive sources (class IIb).

### Description

The Oncentra Prostate system enables a single-step, real-time HDR prostate brachytherapy workflow that aims to reduce both the number and complexity of steps involved in administering the radiotherapy treatment plan. The system provides the clinician with 3D ultrasound guidance to show precisely where in the prostate gland the applicators are inserted, and it gives a clear view of the surrounding organs at risk from the radiation dose. The Oncentra software also provides tools to evaluate the radiotherapy treatment plan and assists in determining the best radiation dose distribution. By combining the imaging and treatment planning software, it eliminates the need to transfer the data to another software planning platform (as is the case when using a non-integrated ultrasound machine for visualising the placement of the applicators). The

treatment plan can be generated before the radiation source is applied and can be changed by adapting the position of the applicators without moving the patient.

The first commercial version of the system (marketed under the name SWIFT) was made available in 2002. Since then, Nucletron has released several versions, the most recent of which (version 4) became available in 2011. The information provided in this briefing relates to version 4.0 of the system and above, referred to as v4.x. NHS clinical oncology departments using the previous version of the system (version 3.x) can upgrade their software without the need to purchase additional hardware (although in some cases a hardware upgrade may be needed).

The Oncentra Prostate system comprises software and hardware components. The software components are:

- Oncentra Prostate treatment planning software
- database software.

The hardware components are:

- The OncoSelect stepper. This controls the ultrasound probe and reports its position to the treatment planning software, enabling a 3D image to be constructed. The OncoSelect stepper also holds the OncoSmart template. The Oncentra Prostate system is also compatible with third-party steppers. Depending on the type of stepper, Nucletron provides adapters for probe fixation.
- The microSelectron HDR, or the more recent Flexitron HDR remote afterloading platform. These are computer-controlled mobile units that contain the radiation source. The Flexitron has up to 40 channels (10, 20 or 40) and is designed to support a standardised workflow with less flexibility to change the treatment variables (such as the offset and the reference length). The microSelectron has up to 30 channels (6, 18 or 30) with higher accuracy of source positioning, and is designed to allow more flexibility and non-standard approaches to treatment.
- OncoSmart single-use applicators or metal reusable applicators. These are used to guide the insertion of the radioactive source inside the prostate.
- The OncoSmart template, used to secure the position of the applicators for insertion into the prostate. The system is also compatible with third-party templates.

- A USB dongle, which is a protection hardware key that prevents unauthorised copying of the software.
- A laptop computer (with docking station) and monitor.
- The EndoCavity Rotational Mover (ECRM), a computer-controlled, motor-driven rotational device used to rotate the ultrasound probe. This is an optional component that is only needed for rotational probe/stepper systems.

Advanced modules are available in addition to the basic Oncentra Prostate software platform. These are developed by MedCom and Pi Medical for Nucletron and provide different levels of functionality, allowing the clinician to optimise the radiotherapy treatment plan. Table 1 lists the radiotherapy planning tools provided by advanced versions of the Oncentra Prostate software (Pi Medical).

**Table 1: Advanced radiotherapy planning features and the Oncentra Prostate software version in which they were first introduced**

Feature	Functionality	Software version
Anatomy-based inverse optimization (VBO)	Radiotherapy planning optimization based on anatomical information	1 and above
DVH-Shaper	A graphical user interface that enables users to interact with the optimization engine	2 and above
Hybrid Inverse Planning and Optimization (HIPO)	Automatic placement of the catheters, defined by the user, in such a way that all selected objectives are realised in the most effective way	3 and above
Multiplan	A toolkit for comparing different brachytherapy treatment plans, by comparing the dose volume histograms or directly the 3D dose distributions	3 and above
Live Automatic Catheter Reconstruction on Ultrasound (LACRUS)	A segmentation algorithm used to track an applicator in real-time whilst it is inserted by the clinician during brachytherapy treatment	4 and above

Advanced shaper	A multi-objective inverse optimization, based on the Dose Volume Histogram representation.	Not clear
-----------------	--	-----------

According to the manufacturer, Oncentra Prostate 4.x software has the following features that were not available in previous versions:

- A radiotherapy treatment plan manager module that automates routine tasks during treatment planning.
- The ability to contour in arbitrary planes.

Table 2 lists the software modules available for installation with version 4.x.

**Table 2: Modules available for installation with Oncentra Prostate software 4.x and their functionality**

Module name	Functionality
Basic module	Main user interface and basic functions
SmoothBase	Patient management and administration database
3D Ultrasound	3D capabilities and ultrasound control
Auto recognition of catheters	Automatic catheter recognition on ultrasound images
Auto contouring	Automatic VOI contouring
Inverse planning	Multi-objective anatomy- and DVH-based optimization and decision tools
RT-HDR William Beaumont	Anatomic placement of catheters using customizable parameters according to the William Beaumont Hospital method
CT/MR and advanced optimizations	Radiotherapy treatment planning using CT and MRI images
Colour US (Doppler)	Support of colour ultrasound imaging for acquisition and planning



Fusion for all modalities	Volume fusion and registration of two volumes
---------------------------	---

## Intended use

The Oncentra Prostate is a real-time ultrasound-guided system intended for HDR brachytherapy in patients with intermediate- or high-risk localised prostate cancer.

## Setting and intended user

HDR brachytherapy with the Oncentra Prostate may be offered as an in-patient treatment in NHS clinical oncology departments equipped to deliver brachytherapy. Patients with intermediate- or high-risk prostate cancer in these centres can have brachytherapy with the Oncentra Prostate either as monotherapy or in combination with EBRT to provide a boost dose.

The system is intended for use by qualified medical personnel suitably trained in brachytherapy procedures. Installation, maintenance, and training support services for the Oncentra Prostate are available from Nucletron.

## Current NHS options

Current NHS options include either active surveillance or radical treatment of intermediate- or high-risk localised prostate cancer. Active surveillance is considered for men with intermediate-risk localised prostate cancer who do not wish to have immediate radical prostatectomy or radiotherapy, as outlined in NICE's guideline on [prostate cancer: diagnosis and treatment](#).

For men with intermediate-risk prostate cancer who wish to have radical treatment, and men with high-risk localised prostate cancer, NICE recommends a combination of radical radiotherapy and androgen deprivation therapy. NICE suggests that these men can be offered HDR brachytherapy with EBRT. Brachytherapy should not be offered as a monotherapy for men with high-risk localised prostate cancer.

The guideline makes no distinction between HDR prostate brachytherapy given as a 1-step (real-time) or 2-step procedure, and the decision will be based on the clinical oncology department's equipment and ability to adopt a single-step technique.

NICE is aware of the following CE-marked device that appears to fulfil a similar function to the Oncentra Prostate:

- Vitesse 3.0 (Varian).

## Costs and use of the technology

Information on the cost of using the technology has been provided by the manufacturer. All costs presented below exclude VAT and were converted from euros to pounds sterling using purchasing power parities and exchange rates (Organisation for Economic Co-operation and Development, September 2014).

The NHS acquisition cost of the Oncentra Prostate depends on whether an older system is being upgraded or an entire new system is being purchased. Both scenarios assume that an ultrasound scanner is already available in the brachytherapy unit. If not, the capital costs associated with a new ultrasound scanner should be added.

The manufacturer states a total cost of £34,250 (excluding VAT) for systems to be upgraded from Oncentra Prostate 3.x to 4.x. The upgrade is mainly related to changes in system software, with some minor hardware upgrades such as increased computer memory. This total includes the following costs:

- Product upgrade (Oncentra Prostate 3.x to Oncentra prostate 4.x): £13,885.
- Laptop cart package to enable hardware upgrade: £20,365.

The total cost of a new Oncentra Prostate 4.x system is £127,657 (excluding VAT and the optional components), including the following individual costs (all prices exclude VAT):

- Oncentra Prostate 4.x: £97,295.
- OncoSelect stepper and stepper encoder: £25,919.
- Adapter set for the OncoSelect stepper: £4443 (other steppers can be used with the system, and the manufacturer provides adapters for probe fixation using different types of stepper).

Costs for optional extra components for either an upgrade or a new system:

- An optional advanced imaging and advanced optimisation system: £19,439.
- EndoCavity rotation mover (ECRM): £3703.

Costs for consumable items used with the Oncentra Prostate system:

- Disposable applicators: during each brachytherapy session, around 16 disposable applicators are used per patient at a total cost of £2222.
- Non-disposable applicators: these can be sterilised and used for more than 1 patient, but are eventually disposed of after approximately 6 months. The cost for 16 non-disposable applicators is £1290.

In addition to hardware and software costs, maintenance costs add up to £18,513 per year (excluding the first year).

Additional hardware costs associated with the Oncentra Prostate system (not included in costs listed above) include the following:

- A HDR source and delivery unit (the afterloader) are required but are not core components of the Oncentra Prostate system. The Oncentra Prostate 4.x is only compatible with Nucletron afterloaders:
  - microSelectron Digital 30 Channels, costing £166,904
  - microSelectron Digital 18 Channels, costing £141,868
  - microSelectron Digital 6 Channels, costing £125,177
  - Flexitron HDR 40 Channels (220–240V), costing £183,593
  - Flexitron HDR 40 Channels (110–120V), costing £183,593
  - Flexitron HDR 20 Channels (220–240V), costing £156,054
  - Flexitron HDR 20 Channels (110–120V), costing £156,054
  - Flexitron HDR 10 Channels (230V), costing £137,695.
- A compatible ultrasound scanner is needed in order to use the Oncentra Prostate 4.x, and this must be purchased separately. The system can be used with commercially available ultrasound systems using a regular video output and bi-plane probe.

Staff must be appropriately trained in order to use the Oncentra Prostate system. Nucletron provides dedicated education and training in the form of peer-to-peer sessions. For example, a combined on-site team training and consulting program is available at an additional cost of £13,073.

The anticipated lifespan of the technology is 10 years. The following assumptions were used to estimate a cost per treatment:

- The technology is used in 240 patients (that is, 1 patient per day for 240 working days per year).
- The duration of a brachytherapy session with the Oncentra Prostate 4.x is estimated to be 2–3 hours.
- Personnel costs as follows: 1 urologist, 1 oncologist and 1 anaesthetist at £139 per hour (Curtis, 2013); 2 physicists at £100 per hour; 1 registered nurse at £100 per hour, 1 technician at £100 per hour and 1 operating department assistant at £21 per hour.
- The use of a brachytherapy room at £200 per hour.
- The re-use of the metal applicators (where used) for a period of 6 months (that is, in 120 patients).
- The annual capital costs were estimated using a standard 'annuity method' with an equipment lifespan of 10 years and a discount rate of 4% (Drummond et al. 2005).

The total cost per treatment if upgrading from the Oncentra Prostate 3.x to the 4.x is £2757 per treatment. The total cost per treatment if a new Oncentra Prostate 4.x is purchased is £2803 per treatment.

No other practical difficulties have been identified in using or adopting the technology. Nucletron provides refresher training for staff performing brachytherapy, ensuring compliance with the technology.

Current standard of care in the NHS is 2-step HDR brachytherapy.

## Likely place in therapy

The Oncentra Prostate is an option for managing intermediate- and high-risk localised prostate cancer needing radical radiotherapy treatment. Different treatment modalities

with various side effects are available for prostate cancer, and so men with prostate cancer should be given the opportunity to discuss their treatment options with specialist surgical and clinical oncologists. If the decision is made to have radical radiotherapy with HDR brachytherapy, then the Oncentra Prostate system can be used to deliver that treatment.

## Specialist commentator comments

All specialist commentators agreed that single-step HDR brachytherapy with the Oncentra Prostate system would save time compared with conventional 2-step HDR brachytherapy treatment. However, they were not able to estimate how much time could be saved. They noted that an experienced brachytherapy team needed 2–3 hours to complete the single-step real-time procedure with the Oncentra Prostate, compared with approximately 6 hours to complete the 2-step procedure (from administration of anaesthetic in theatre to the removal of the applicators).

Two commentators stated that although the total procedural time would be reduced, the overall length of hospital stay would not be significantly shortened using a single-step real-time approach with the Oncentra Prostate. This is because the patient would have to stay in hospital overnight regardless of the length of the procedure, because it is recommended that the patient stays in hospital until the urinary catheter is removed (the urinary catheter is only removed when the patient's urine becomes clear of blood, and the time taken to reach this stage would be no different for single-step or 2-step HDR brachytherapy). However, 1 specialist commentator felt that the total procedure time would be reduced by 3–4 hours and could potentially avoid the need for the patient to stay in hospital overnight.

Three commentators noted that because single-step real-time HDR brachytherapy is done in a single room, the risk of applicators being dislodged is lower than with the 2-step procedure. They commented that treatment delivery is more accurate when there is no movement of the applicators and when the overall procedural time is reduced.

Two commentators noted that the single-step real-time process is more straightforward because there is no dependence on the availability of a CT or MRI scanner, and the patient does not need to be transferred to another room. Because no CT or MRI is needed, using the Oncentra Prostate system would reduce the number of staff involved in the procedure and therefore reduce the associated costs.

One commentator noted that the microSelectron HDR and the Flexitron HDR afterloaders can be used to treat other cancer sites, which may offset the additional costs in departments that share these resources for treating different cancer types. The same commentator also noted that the Oncentra Prostate 4.x can be used for low-dose rate seed implant prostate brachytherapy. One specialist commentator stated that the Oncentra Prostate system is also compatible with third-party steppers and templates.

All of the commentators confirmed that there are only minor changes between the Oncentra Prostate v4.x and v3.x. In terms of hardware, these changes are mainly the introduction of sagittal ultrasound acquisition support, which improves the image quality and therefore speed and accuracy. In terms of the software, the changes between the 2 versions are mostly improvements to existing features rather than major changes that would affect patient outcomes. In general, the changes make the system more user-friendly, potentially more accurate and faster.

## Equality considerations

NICE is committed to promoting equality and eliminating unlawful discrimination. We aim to comply fully with all legal obligations to:

- promote race and disability equality and equality of opportunity between men and women, and
- eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief, in the way we produce our guidance (these are protected characteristics under the Equality Act [2010]).

Men aged over 50 years and men of African-Caribbean family origin are both at increased risk of prostate cancer. Age and race are protected characteristics defined in the Equality Act (2010).

## Patient and carer perspective

Single-step real-time HDR brachytherapy is a safe and effective procedure. However, as with most cancer treatments, there are some risks associated with HDR brachytherapy with EBRT. It is therefore important that all men offered this treatment discuss the benefits and side effects with their doctor and clinical team. They can then make an informed

decision about their treatment.

The long-term risks associated with the procedure are:

- impotence (problems with getting and keeping an erection)
- narrowing of the urethra and thus difficulty in passing urine
- proctitis (inflammation of the back passage).

More detailed information on these risks can be found in CRUK's guide on prostate brachytherapy (Cancer Research UK, 2014b).

## Evidence review

### Clinical and technical evidence

#### Regulatory bodies

Two incidents were identified in the US Food and Drug Administration (FDA) database: Manufacturer and User Device Facility Experience (MAUDE), both of which were attributed to system malfunctions. Neither of the incidents resulted in any patient being harmed. In the first, Oncentra Prostate v3.09 malfunctioned 6 times during treatment, resulting in a delay to the patient's second brachytherapy fraction. In the second incident, a radiotherapy treatment plan was optimized twice with the dose volume histogram-based optimization algorithm, with inconsistent results. The version of the system used during this incident is not known ([MAUDE Adverse Event Report: Nucletron BV Oncentra Prostate \[SWIFT\] treatment planning](#)).

#### Clinical evidence

Many of the advanced radiotherapy planning features of the system included in v4.x were initially licensed in v3.x, so this evidence review focuses on the Oncentra Prostate v3.x and above. A literature search identified 1 study of the Oncentra Prostate v4.x and 3 of the Oncentra Prostate v3.x:

- Gomez-Iturriaga et al. (2014, table 4)



- Pokharel et al. (2013, table 5)
- Choudhury et al. (2014, table 6)
- Adamczyk et al. (2013, table 7).

In addition, 7 conference abstracts investigating the Oncentra Prostate system were identified, although the version used was not always reported. These abstracts are summarised and presented in table 3.

## Feasibility studies

Three feasibility studies of the Oncentra Prostate system were identified. All 3 of these were small, single-centre studies analysing technical parameters of radiotherapy planning, mainly the radiation dose delivered to the prostate and the surrounding healthy organs at risk of radiation exposure.

Pokharel et al. (2013) investigated the effectiveness of the hybrid inverse planning and optimization (HIPO) algorithm for real-time HDR brachytherapy in 20 men. The HIPO algorithm is a feature of v3.x and v4.x of the Oncentra Prostate system. It is a user-independent optimisation algorithm, which automatically calculates the best distribution of the applicators (dwell positions and dwell times) to create the radiotherapy treatment plan. Pokharel et al. compared the HIPO algorithm with the graphical optimization (GRO) algorithm, which needs manual adjustment of the isodose lines (these are virtual lines which the software draws on the clinical images to show the areas of tissue that receive different levels of the prescribed radiation dose) to create the radiotherapy treatment plan. The study found that HIPO can provide the same prescribed dose to the prostate as GRO, but with a statistically significant reduction in the dose received by the surrounding organs at risk (urethra, bladder and rectum).

Adamczyk et al. (2013) presented a small, single-centre study of prostate cancer in 15 men. The effect of 3 different automatic optimisation algorithms on treatment plan quality during 3D-conformal real-time HDR brachytherapy was investigated. The 3 algorithms were geometrical optimization, inverse optimization and blind inverse optimization, which are all available with Oncentra Prostate v3.0.9. The authors concluded that the blind inverse optimization algorithm achieved adequate radiation dose for the prostate and the surrounding organs at risk of radiation damage. Although the geometrical optimization algorithm delivered smaller doses to the urethra, this was also associated with a lower therapeutic dose to the prostate.



Gomez-Iturriaga et al. (2014) reported results from a single-centre study on the effect of an intraoperative MRI/transrectal ultrasound (TRUS) fusion procedure in 9 men with extracapsular extension prostate cancer (clinical tumour stage 3a) who had real-time HDR brachytherapy. Real-time MRI/TRUS fusion can be done using the 'Fusion for all modalities' module of the Oncentra Prostate v4.x. The authors analysed men with intermediate- and high-risk prostate cancer who had a single HDR fraction of 15 Gy followed by EBRT at a dose of 37.5 Gy delivered in 15 fractions over 3 weeks. For each participant, 2 virtual treatment plans were developed based on the MRI/TRUS fusion images. These treatment plans were only generated to test the capabilities of the software, and were not used for treatment. According to their findings, MRI contributed additional information for the prediction of extracapsular extension disease and the authors concluded that it should be used for high-risk patients having HDR brachytherapy. One of the authors is also the principal investigator of an ongoing prospective study investigating the feasibility of MRI/TRUS fusion during dose-escalation prostate brachytherapy (ClinicalTrials.gov identifier: NCT01909388), but it should be noted that the Gomez-Iturriaga et al. (2014) study is not a preliminary report of the data from this ongoing prospective trial.

## Cohort study

Choudhury et al. (2014) provides a large UK-based prospective series reporting patient-reported outcomes and health-related quality of life for patients having HDR brachytherapy with the Oncentra Prostate v3.x and hypofractionated EBRT. All patients had androgen-deprivation therapy before and after their radiotherapy treatment. They had a single brachytherapy fraction of 12.5 Gy and 15 fractions of EBRT at 37.5 Gy, starting 2 weeks after brachytherapy. Patients completed postal questionnaires at various time points before and after their treatment. There were no statistically significant associations between dosimetric parameters and patient-reported outcomes. The radiotherapy treatment schedule used was associated with a temporary effect on health-related quality of life and acceptable rates of urinary and bowel side effects.

## Table 3 Summary of abstracts reporting data on the Oncentra Prostate system

Study	Population	Intervention	Outcome measure	Conclusion
-------	------------	--------------	-----------------	------------

Challapalli et al. (2011)	30 men with high risk localised/ locally advanced prostate cancer.	Oncentra Prostate (version number was not described). All men had EBRT (46 Gy) + HDR (12.5 Gy).	Treatment time and dose coverage of the CTV.	Real-time ultrasound planning was a safe and well-tolerated method for increasing the prescribed radiation dose to the prostate whilst not exceeding the dose tolerance of the surrounding organs at risk.
Filipowski et al. (2011)	190 men with stage T1–T2c prostate cancer, mean age=68 years, mean PSA=11.069 ng/ml, Gleason score range 3–7 .	SWIFT 2.11.8 and Oncentra Prostate v3.0.9 and v4.0. 60 men who had EBRT (30 Gy) with HDR (30 Gy) and 130 with HDR (45 Gy) only.	Early treatment side effects and radiation dose received by the CTV and organs at risk.	The majority of patients tolerated the treatment well with acceptable levels of acute side effects.

Kabacinska et al. (2013)	77 men (no information on patient characteristics was provided).	Oncentra Prostate v3.2.3. Most men had EBRT (no information on dose in Gy) with HDR (20 Gy) and the rest had HDR (31.5 Gy) only.	Radiation dose received by the CTV and organs at risk.	The use of anatomy-based inverse optimization followed by graphic optimization during the radiotherapy treatment plan with the system fulfils almost all brachytherapy dosimetric recommendations of ESTRO and ABS guidelines.
--------------------------	--	--	--	--

<p>Kanikowski (2013)</p>	<p>103 men (no information on patient characteristics was provided).</p>	<p>SWIFT and Oncentra Prostate (version number was not described). 37 men had EBRT (50 Gy) with HDR (1 session at 15 Gy), 36 men had EBRT (46 Gy) with HDR (2 sessions at 10 Gy) and 30 men had HDR (3 sessions at 15 Gy) only.</p>	<p>Radiation dose received by the CTV and organs at risk.</p>	<p>Although the same prostate dosimetric parameters were achieved with all 3 different radiotherapy treatment schedules, the HDR brachytherapy schedule using 2 brachytherapy fractions resulted in higher doses received by the organs at risk and lower doses by the prostate.</p>
<p>Kunhiparambath et al. (2011)</p>	<p>5 men (no information on patient characteristics was provided).</p>	<p>Oncentra Prostate (version number was not described).</p>	<p>Radiation dose received by the PTV and organs at risk.</p>	<p>Single objective dose volume histogram-based inverse planning optimization is superior to volume-based geometric optimization.</p>

Laviraj et al. (2011)	4 men with (no information on patient characteristics was provided).	Oncentra Prostate (version number was not described).	Dosimetric parameters.	Better dose coverage of the prostate and almost the same dose to healthy organs at risk were achieved with the multisolution dose volume histogram-based algorithm in comparison with the multisolution variance-based optimization algorithm.
Schwarz et al. (2010)	36 men with intermediate- or high-risk prostate cancer.	Oncentra Prostate (version number was not described). All men had EBRT (50.4 Gy) with HDR (9 Gy).	Radiation dose received by the CTV and organs at risk.	Oncentra Prostate Nucletron brachytherapy system was successfully implemented in daily routine. The 3D-treatment optimization showed excellent dose parameters in accordance to the radiotherapy treatment plan objectives.
Abbreviations: ABS, American Brachytherapy Society; CTV, clinical target volume; ESTRO, European Society for Radiology and Oncology; PTV, planning target volume.				

**Table 4 Summary of the Gomez-Iturriaga et al. (2014) single-centre feasibility study**

Study component	Description
-----------------	-------------

Objectives/ hypotheses	To evaluate the impact of intraoperative MRI/TRUS fusion in patients with cT3a prostate cancer treated with high-dose-rate real-time brachytherapy.
Study design	A retrospective, single-centre, feasibility study.
Setting	Spain
Inclusion/ exclusion criteria	Inclusion criteria: <ul style="list-style-type: none"> <li>• proven adenocarcinoma of the prostate;</li> <li>• clinical (MR imaging) stage T3a disease and</li> <li>• without clinical or radiographic evidence of metastases</li> </ul>
Primary outcomes	All outcomes were presented as mean figures. <ul style="list-style-type: none"> <li>• Prostate dose volume histograms</li> <li>• Extracapsular extension (ECE)</li> <li>• Maximal urethral and rectum dose</li> </ul>
Statistical methods	Comparisons of the mean values between the 2 plans were done using the paired t-test. Significance was defined as a probability value less than 0.05, and no adjustment was made for multiple comparisons.
Participants	9 consecutive patients participated in this study, mean age=68 years (range 60–78), intermediate-risk=6, high-risk=2, very high risk=1.
Results	<p>Mean radial distance of ECE was 3.6 mm (SD: 1.1).</p> <p>No significant differences were found between prostate V100, V150, V200, and OARs DVH-related parameters between the plans.</p> <p>Mean values of ECE V100, V150, and V200 were 85.9% (SD: 15.1), 18.2% (SD: 17.3) and 5.85% (SD: 7) respectively when the doses were prescribed to the PTVUS.</p> <p>Mean values of ECE V100, V150, and V200 were 99.3% (SD: 1.2), 45.8% (SD: 22.4) and 19.6% (SD: 12.6) respectively when doses were prescribed to PTVMR</p> <p>(p=0.028, p=0.002 and p=0.004 respectively).</p>

Conclusions	TRUS/MRI fusion provides valuable information for prostate brachytherapy, allowing delivery of a higher dose and better target coverage of extracapsular disease in patients with clinical stage T3a.
Abbreviations: CI, confidence interval; DVHO, dose-volume histogram-based optimization; GRO, graphical optimization; HIPO, hybrid Inverse treatment planning; ITT, intention to treat; n, number of patients; RR, relative risk; TRUS, transrectal ultrasound.	

**Table 5 Summary of the Pokharel et al. (2013) single-centre feasibility study**

Study component	Description
Objectives/hypotheses	To investigate the effectiveness of the HIPO planning and optimization algorithm for real-time prostate HDR brachytherapy.
Study design	A retrospective, single-centre, feasibility study.
Setting	USA-based. Recruitment period: March 2007 to October 2009.
Inclusion/exclusion criteria	No specific criteria were presented.
Primary outcomes	<ul style="list-style-type: none"> <li>• PTV</li> <li>• PTV to OARs (urethra, rectum, bladder, and normal tissue)</li> <li>• HI</li> <li>• COIN.</li> </ul>

Statistical methods	<p>The paired student t-test (<math>p &lt; 0.05</math>) was used to make statistical comparisons of different dosimetric quality indices of treatment plans optimized by different optimization algorithms.</p> <p>The statistical comparisons were:</p> <ul style="list-style-type: none"> <li>• HIPO1 vs GRO</li> <li>• HIPO1 vs HIPO2</li> <li>• HIPO1 vs DVHO.</li> </ul> <p>The comparison between HIPO and DVHO with the same weighting factors was carried out to investigate the importance of dwell position optimization.</p>
Participants	20 patients: the authors do not provide any further information regarding patient characteristics.
Results	The PTV receiving 100% of the prescription dose (V100) was 95.38% with HIPO and 97.56% with GRO. The mean dose and minimum dose to 10% volume for the urethra, rectum, and bladder were all statistically lower with HIPO compared with GRO using the paired student t-test at 5% significance level.
Conclusions	HIPO can provide treatment plans with comparable target coverage to that of GRO with a reduction in dose to the critical structures.
<p>Abbreviations: CI, confidence interval; COIN, conformal index; DVHO, dose-volume histogram-based optimization; GRO, graphical optimization; HI, homogeneity index; HIPO, hybrid inverse treatment planning; ITT, intention to treat; n, number of patients; RR, relative risk.</p>	

**Table 6 Summary of the Choudhury et al. (2014) single-centre cohort study**

Study component	Description
Objectives/hypotheses	To investigate the effect of HDR brachytherapy combined with EBRT on patient-reported outcomes and health-related quality of life.



Study design	<p>A prospective, single-centre, cohort study.</p> <p>Patients completed postal questionnaires after an initial consultation (baseline), immediately before attending for HDR brachytherapy (pre-treatment), and after EBRT at 6 weeks and 6, 12, 18, 24 and 36 months.</p>
Setting	<p>The Christie NHS Foundation Trust, UK.</p> <p>Recruitment period: July 2008 to March 2010.</p>
Inclusion/exclusion criteria	<p>Patients presenting with histologically confirmed intermediate- or high-risk prostate cancer according to the D'Amico classification were considered eligible for HDR brachytherapy combined with hypofractionated EBRT. All patients were staged using cross-sectional pelvic imaging and an isotope bone scan to exclude metastases.</p> <p>Exclusion criteria: prostate-specific antigen &gt;100, IPSS &gt;20, history of previous transurethral resection of the prostate, and contraindications to general anaesthesia.</p> <p>No specific prostate volume constraints were applied within this group of patients.</p>
Primary outcomes	<p>Patient-reported toxicity data:</p> <ul style="list-style-type: none"> <li>• IPSS</li> <li>• LENT-SOMA questionnaires.</li> </ul> <p>Health-related quality of life data:</p> <ul style="list-style-type: none"> <li>• EPIC questionnaire.</li> </ul>

<p>Statistical methods</p>	<p>The mean and median IPSS were calculated at each time-point. LENT-SOMA data were presented as an overall mean and median score for each anatomical subscale in addition to the proportion of patients reporting a score of 2 for a single question within each subscale.</p> <p>The EPIC questionnaire was analysed using the mean, median and interquartile range for the urinary, bowel, sexual and hormonal domains and their subdomains. A change of <math>\leq 10\%</math> in the EPIC score was considered to be clinically significant.</p> <p>Median scores at each time-point were compared from baseline using the Wilcoxon matched-pairs signed-rank test and a 2-sided <math>p</math>-value <math>\leq 0.01</math> (Bonferroni correction made for multiple comparisons).</p> <p>Spearman's rank coefficient was used to investigate any associations between patient clinical factors and dose parameters at HDR planning and subsequent toxicity.</p>
<p>Participants</p>	<p>95 men with intermediate- or high-risk prostate cancer, median age=68 (range=51–78) years, median prostate-specific antigen=16.7 (range=0.29–90) ng/ml.</p>
<p>Results</p>	<p>95 men had an HDR boost of 12.5 Gy followed by EBRT delivered as 37.5 Gy in 15 sessions over 3 weeks.</p> <p>The IPSS peaked 6 weeks after radiotherapy (median=9).</p> <p>The LENT-SOMA bladder/urethra mean baseline score was 0.35 and peaked 6 weeks after radiotherapy (mean=0.59).</p> <p>Difficulties with urinary flow and frequency were the most common reported symptoms.</p> <p>LENT-SOMA rectum/bowel mean scores at baseline were 0.24 and peaked after 6 months (mean=0.37).</p> <p>Bowel urgency was the most common reported toxicity.</p> <p>EPIC urinary scores returned to baseline values at 6 months and bowel median scores recovered after 24 months.</p> <p>There were no statistically significant associations between patient or dosimetric parameters and patient-reported outcomes.</p>

Conclusions	A combined HDR boost and hypofractionated EBRT regimen offers a well-tolerated method of dose escalation with acceptable levels of patient reported toxicity.
Abbreviations: CI, confidence interval; , EPIC, Expanded Prostate Cancer Index Composite; IPSS, International Prostate Symptom Score; ITT, intention to treat; LENT-SOMA, Late Effects in Normal Tissues-Subjective, Objective, Management and Analytic scales; n, number of patients; RR, relative risk	

**Table 7 Summary of the Adamczyk et al. (2014) single-centre feasibility study**

Study component	Description
Objectives/ hypotheses	To present the effect of different optimization algorithms (BIO and GO) on treatment plan quality during 3D-conformal real-time HDR brachytherapy.
Study design	A retrospective, single-centre, feasibility study.
Setting	Poland.
Inclusion/ exclusion criteria	The authors provided no information on inclusion/exclusion criteria.
Primary outcomes	Differences between dose distributions were tracked using: D90, V100, V200, Dmax (for prostate); D10, Dmax (for urethra); D10, V100, Dmax (for rectum).
Statistical methods	The analysis of each index was done by dividing the data into 3 groups depending on the algorithm used in the optimization process. Statistical differences between groups were verified using t-test and Wilcoxon's test.  Differences between groups were considered significant if the p-value was <0.05.
Participants	15 patients (no information provided on patient characteristics).

Results	<p>The analysis of mean values of D90 and V100 in the prostate showed that inverse algorithms gave the best results (mean D90 was 12.1% greater for BIO and 9.3% greater for IO compared with GO, mean V100 was 8.2% greater for BIO and 6.3% greater for IO compared with GO).</p> <p>From a clinical point of view, GO diminished the doses in the PTV and urethra in all analysed parameters. The lowest mean doses in the rectum were achieved for plans optimized with IO and BIO (mean D10: 61.2% for GO, 58.1% for IO, 58.0% for BIO; mean Dmax: 92.8% for GO, 85.1% for IO, 83.6% for BIO).</p>
Conclusions	<p>Application of the BIO algorithm led to clinically best dose parameters for PTV and the rectum. Use of GO led to smaller doses in the urethra, which was however associated with a dose decrease in the PTV.</p>
<p>Abbreviations: BIO, blind inverse optimization; CI, confidence interval; D10, dose covering 10% of the urethral or rectal volume; D90, the dose (in Gy or as a percentage of the prescription dose) that covers 90% of the prostate volume; Dmax, the maximum dose received by the prostate and organs at risk; GO, geometrical optimization; ITT, intention to treat; n, number of patients; PTV, planning target volume; RR, relative risk; V100, the fractional volume of the prostate that receives 100% of the prescription dose; V200, the fractional volume of the prostate that receives 200% of the prescription dose.</p>	

## Recent and ongoing studies

One ongoing trial using the Oncentra Prostate v4.x was identified (ClinicalTrials.gov identifier: NCT01909388). The BRAPOST trial (Dose Escalation to Dominant Intraprostatic Lesions With MRI-TRUS Fusion HDR Prostate Brachytherapy) started in July 2013 and at the time of writing is recruiting patients. The estimated completion date is July 2016.

## Costs and resource consequences

No published evidence on resource consequences of the Oncentra Prostate was identified in the systematic review of evidence.

The Oncentra Prostate v4.x is intended to replace the use of CT imaging in the planning and delivery of HDR brachytherapy treatment, and this would have the greatest resource and planning consequences for brachytherapy units that currently do not use real-time

single-step brachytherapy. These consequences include potentially decreased procedural time and releasing CT and MRI imaging facilities for use by other patients.

The manufacturer states that 7 NHS clinical oncology departments are currently using the Oncentra Prostate system.

## Strengths and limitations of the evidence

Real-time ultrasound-guided HDR brachytherapy with the Oncentra Prostate system is designed for men who have been diagnosed with intermediate- or high-risk localised prostate cancer. Although the patients included in the Gomez-Iturriaga et al. (2014) and Choudhury et al. (2014) studies were men with intermediate- or high-risk localised prostate cancer, Pokharel et al. (2013) and Adamczyk et al. (2013) do not provide any information regarding the risk status of the men included in their studies. As a result, it is unclear whether their study populations match the intended use of the system.

The Pokharel et al. study reported the results of a retrospective, single-centre study of 20 men with prostate cancer. It should be noted that the small sample size and parametric statistical methods employed may reduce the statistical power of this study. The publication made no mention of data distribution or normality. Given the small sample size, these factors should have been considered or non-parametric testing should have been used. The primary outcome measures of the study investigated the effectiveness of the HIPO algorithm in technical aspects of radiotherapy treatment planning. The absence of long-term follow-up means that only limited conclusions can be drawn on the effect of the achieved dosimetric parameters with the HIPO algorithm (as compared with GRO) on patient-related outcomes including survival, biochemical control or health-related quality of life measures. Although some data suggest a relationship between radiation dose and patient outcome measures, including survival, the strength of these conclusions is often limited by the small sample sizes of these studies, the incompleteness of the data, and the presence of bias in non-randomised studies (van Tol-Geerdink 2006).

The Adamczyk et al. (2013) study presented a single-centre, small sample size (n=15) study investigating the effect of 3 different optimisation algorithms on radiotherapy treatment planning. The authors provided no information on either patient characteristics or the exact treatment that patients had. Adamczyk et al. failed to demonstrate statistically significant differences between all outcomes, which may be a result of a small sample size.

Choudhury et al. (2014) presented their single-centre experience using a combination of EBRT and real-time HDR brachytherapy (a boost approach), describing the toxicity and quality of life effects associated with the combination. Compared with the other studies reviewed in this briefing, this prospective single-centre study had a larger sample size (n=95) and presents outcome measures relating to patient-reported quality of life. There were no statistically significant associations between clinical characteristics or dosimetric parameters and patient-reported outcomes. The patient-reported outcome data were strengthened because the authors used a validated questionnaire (LENT-SOMA) for their analysis, assessed the outcomes at various time points, and had a long-term follow-up. However, patient-reported measures may introduce bias because of overestimation or subjectivity. The authors also noted that although questionnaires return rates were over 50% at every time point, they were not always fully completed. In this study, p-values were adjusted to reduce the risk of false-positive results arising simply because a large number of comparisons were made. However, this will also increase the likelihood of false-negative results. Details of the correction and of the p-values prior to correction were not provided.

The study by Gomez-Iturriaga et al. (2014) was limited, because their analysis was of a small number of men and included only dosimetric parameters. Nevertheless, their prospective study was planned to report patient-related outcomes on acute side effects, treatment tolerability and efficacy (assessed by biochemical control, MRI and biopsy results) with long-term follow-up at 12, 24 and 30 months after treatment.

A number of abstracts were also identified in the literature search. These abstracts did not report full information on study design or patient characteristics. It also was not always possible to confirm which version of the Oncentra Prostate was used in each study. The abstract by Filipowski et al. (2011) was the only one of these to specify that v4.x was used, but this version was not used for the entirety of the study. Generally, all abstracts included in this briefing reported improvements in radiotherapy treatment planning dosimetric parameters associated with the use of the Oncentra Prostate system. However, only limited data on patient-related outcomes were available. Overall, the abstracts reported that HDR brachytherapy with the Oncentra Prostate was safe and well tolerated. Two deaths were reported among the 190 men enrolled in the Filipowski et al. study, but the authors provided no information as to the causes.

The Filipowski et al. abstract highlighted the need for longer follow-up data, specifically related to survival and toxicity. This applies equally to all of the studies reviewed in this briefing.

In general, the studies included in this briefing focused on technical aspects of treatment delivery rather than patient outcomes. Choudhury et al (2014) is the only study to address clinical outcomes, but even in this case treatment tolerability rather than efficacy is measured.

The manufacturer claims that ultrasound treatment planning of real-time single-step HDR brachytherapy using the Oncentra Prostate system results in a reduction in the length of the procedure time compared with a 2-step process. However, no published evidence was found to support this. The use of automated optimisation algorithms can potentially reduce the time needed to find the best radiotherapy treatment plan and improve the dosimetric parameters (Pokharel et al. 2013, Adamczyk et al. 2013), but data on the actual impact on the overall procedure time are not available.

The majority of identified evidence relates to previous versions of the Oncentra Prostate rather than the currently available v4.x. No published evidence directly comparing the performance of the v4.x with previous versions has been identified. As a result, conclusions on improved dosimetric or patient-related outcomes between the new and older versions cannot be formed.

## Relevance to NICE guidance programmes

- [Prostate cancer: diagnosis and treatment](#) (2014) NICE guideline CG175

## References

Adamczyk M, Zwierzchowski G, Malicki J, et al. (2013) [Evaluation of clinical benefits achievable by using different optimization algorithms during real-time prostate brachytherapy](#). *Physica Medica* 29: 111–6

Batchelar DL, Law N, Cisecki T, Loblaw DA, Chung H, Morton GC (2011). [Does Intraoperative Ultrasound-Based Planning for HDR Prostate Brachytherapy Reduce Needle Displacement?](#) *Brachytherapy* 10, Supplement 1(0): S92

Cancer Research UK (2014a) [Prostate cancer key facts](#) [accessed September 2014]

Cancer Research UK (2014b) [Internal radiotherapy \(brachytherapy\) for prostate cancer](#) [accessed September 2014]



Challapalli A, Robinson A, Dunn P, et al. (2011) Image guided HDR brachytherapy boost for locally advanced prostate cancer using OnCentra™ prostate HDR planning system *Clinical Oncology*. Conference: UK Radiation Oncology Conference 2011 Manchester United Kingdom. Conference Publication: 23 (3) (pp S14), 2011

Choudhury A, Arthur C, Malik J, et al. (2014) Patient-reported Outcomes and Health-related Quality of Life in Prostate Cancer Treated with a Single Fraction of High Dose Rate Brachytherapy Combined with Hypofractionated External Beam Radiotherapy. *Clinical Oncology*; in-press

Curtis L (2013) PSSRU: Unit Costs of Health & Social Care 2013

Drummond M, Sculpher M, Torrance G, et al. (2005) *Methods for economic health evaluation of health care programmes* (3rd ed.) Oxford University Press

Filipowski TM, Szmigiel-Trzcinska A, Topczewska-Bruns J, et al. (2012) Efficacy, toxicity and dosimetric aspects of HDR brachytherapy in prostate cancer patients: 5 years experience. *Radiotherapy and Oncology*. Conference: World Congress of Brachytherapy, Barcelona Spain. Conference Publication: 103 (pp S72), 2012

Gomez-Iturriaga A, Crook J, Casquero F et al. (2014) Impact of intraoperative MRI/TRUS fusion on dosimetric parameters in cT3a prostate cancer patients treated with high-dose-rate real-time brachytherapy. *Journal of Contemporary Brachytherapy* 6(2): 154–160

Kabacinska R, Terlikiewicz J, Lasota J, et al. (2013) Evaluation of dosimetric parameters in prostate high-dose-rate brachytherapy: Applicability of anatomybased inverse optimization and graphic optimization. *European Urology, Supplements* 12 (6): 162

Kanikowski M (2013) Comparison of treatment plan parameters in brachytherapy of prostate cancer in different schedules. *Brachytherapy*. Conference: 34th Annual Meeting of the American Brachytherapy Society, ABS 2013 New Orleans, LA United States. Conference Publication: 12 (pp S64), 2013

Kunhiparambath H, Laviraj MA, Rath GK, et al. (2011) A comparative analysis of single objective dose volume histogram (SDVHO)-based inverse planning optimization versus volume-based geometric optimization in real-time prostate brachytherapy planning with OnCentra™ Prostate. *Journal of Clinical Oncology*. Conference: ASCO Annual Meeting 2011 Chicago, IL United States. Conference Publication: 29 (15 SUPPL. 1), 2011.



Laviraj MA, Rath GK, Kunhiparambath H, et al. (2011) Multisolution variance-based optimization (MVBO) versus multisolutions dose volume histogram-based optimization (MDVHO): A comparative analysis of anatomy-based multisolution blind inverse planning optimizations in OnCentra™Prostate. Journal of Clinical Oncology. Conference: ASCO Annual Meeting 2011 Chicago, IL United States. Conference Publication: 29 (15 SUPPL. 1), 2011

Milickovic N, Mavroidis P, Tselis N, Nikolova I, Katsilieri Z, Kefala V, Zamboglou N, Baltas D (2011) 4D analysis of influence of patient movement and anatomy alteration on the quality of 3D U/S-based prostate HDR brachytherapy treatment delivery. Medical Physics 38(9): 4982–93

Pi Medical (2014) Product development [accessed September 2014]

Pokharel S, Rana S, Blikenstaff J, et al. (2012) Evaluation of hybrid inverse planning and optimization (HIPO) algorithm for optimization in real-time, high-dose-rate (HDR) brachytherapy for prostate. Journal of Applied Clinical Medical Physics 14(4): 4198

Schwarz R, Thurmann H, Lambert J, Frenzel T, Platz V, Petersen C, Krüll A (2010) Implementation of a new brachytherapy planning and delivery system in the daily routine of HDR-brachytherapy of prostate cancer. Strahlentherapie Onkologie 186(1): 148

Sedgwick P (2012) Multiple significance tests: the Bonferroni correction. British Medical Journal 344: e509

van Tol-Geerdink JJ, Stalmeier PFM, Pasker-de Jong PCM, Huizenga H, van Lin E, Schimmel C, Leer JW, van Daal W (2006).Systematic review of the effect of radiation dose on tumor control and morbidity in the treatment of prostate cancer by 3D-CRT. International Journal of Radiation Oncology Biology Physics 64(2): 534–43

## Search strategy and evidence selection

Embase 1980 to 2014 Week 34, Ovid MEDLINE In-Process & Other Non-Indexed Citations and Ovid MEDLINE 1946 to Present; 744 references were returned on 10 September 2014. The search strategy was:

1. Oncentra

2. Nucletron

3. brachytherapy

4. HDR

5. High Dose Rate

6. 4 or 5

7. 3 and 6

8. real-time ultrasound

9. 1 or 2 or 7 or 8

10. prostate

11. 9 and 10

12. Limit to English language, limit to human and year 2007 to current

13. Remove duplicates

The search strategy for the Cochrane and DARE databases was:

- Any field: Oncentra/ OR
- Any field: HDR Brachytherapy/OR
- Any field: Prostate Cancer

## Evidence selection

Total number of publications reviewed: 744

Total number of publications considered relevant: 41 (28 full publications and 13 abstracts)

Total number of publications selected for inclusion in this briefing: 11 (4 full publication and 7 abstracts)

Exclusion criteria: case studies, editorials, letters, reviews, animal studies, and non-English language studies, not using the Oncentra Prostate system v3.0 and above.

## Search strategy and evidence selection (economic)

Embase 1980 to 2014 Week 34, Ovid MEDLINE In-Process & Other Non-Indexed Citations and Ovid MEDLINE 1946 to Present. Searched on 4 September 2014

1. prostate.mp.
2. brachytherapy.mp. or Brachytherapy/
3. HDR.mp.
4. High Dose Rate.mp.
5. real-time ultrasound.mp.
6. OnCentra.mp.
7. Nucletron.mp.
8. 2 or 3 or 4 or 5 or 6 or 7
9. cost\*.mp.
10. economic\*.mp.
11. 9 or 10
12. 1 and 8 and 11
13. limit 12 to English language

14. limit 13 to year="2007 -Current"

15. limit 14 to humans

16. remove duplicates from 15

Cochrane Database of Systematic Reviews Issue 9 of 12, September 2014

Cochrane Central Register of Controlled Trials Issue 8 of 12, August 2014

1. Oncentra or HDR Brachytherapy

2. Prostate Cancer

3. cost\* or economic\*

4. #1 and #2 and #3

DARE (Database of Abstracts of Reviews of Effects), NHS EED (National Health Service Economic Evaluation Database), and HTA (Health Technology Assessment) databases; Searched on 4 September 2014

(Oncentra or HDR Brachytherapy ) AND (Prostate Cancer ) AND (cost\* or economic\* ) IN DARE, NHSEED, HTA FROM 2007 TO 2014

## Evidence selection (economic)

Total abstracts: 239

Duplicates: 1

Abstracts reviewed: 238

Full papers reviewed: 0

Exclusion criteria: case studies, editorials, letters, reviews, conference proceedings/ abstracts, animal studies, non-English language studies, not using the Oncentra Prostate.

Studies for review: 0

## About this briefing

Medtech innovation briefings summarise the published evidence and information available for individual medical technologies. The briefings provide information to aid local decision-making by clinicians, managers, and procurement professionals.

Medtech innovation briefings aim to present information and critically review the strengths and weaknesses of the relevant evidence, but contain no recommendations and **are not formal NICE guidance**.

## Development of this briefing

This briefing was developed for NICE by King's Technology Evaluation Centre. The [interim process and methods statement](#) sets out the process NICE uses to select topics, and how the briefings are developed, quality assured and approved for publication.

## Project team

- King's Technology Evaluation Centre (KiTEC), King's Health Partners
- Medical Technologies Evaluation Programme, NICE

## Peer reviewers and contributors

- Anastasia Chalkidou, Health Technology Assessor, KiTEC
- Robert Dowling, Health Technology Assessor, KiTEC
- Tiago Rua, Health Economist, KiTEC
- Muralikrishnan R. Kartha, Health Economist, KiTEC
- Stephen Keevil, Director, KiTEC
- Cornelius Lewis, Director, KiTEC
- Viktoria McMillan, Centre Manager, KiTEC

## Specialist commentators

The following specialist commentators provided comments on a draft of this briefing:

- Dr John Logue, Clinical Oncologist, The Christie NHS Foundation Trust
- Dr Simon Russell, Clinical Oncologist, Cambridge University Hospitals NHS Foundation Trust
- Dr Joshua Mason, Medical Physicist, St. James's University Hospital, Leeds
- Robert Johnstone, Medical Physicist, Guy's and St Thomas' NHS Foundation Trust

## Copyright

© National Institute for Health and Care Excellence 2014. All rights reserved. NICE copyright material can be downloaded for private research and study, and may be reproduced for educational and not-for-profit purposes. No reproduction by or for commercial organisations, or for commercial purposes, is allowed without the written permission of NICE.

ISBN: 978-1-4731-0870-7