Australian Government

Department of Health and Ageing

Australia and New Zealand Horizon Scanning Network

ANZHSN

AN INITIATIVE OF THE NATIONAL, STATE AND TERRITORY GOVERNMENTS OF AUSTRALIA AND THE GOVERNMENT OF NEW ZEALAND

National Horizon Scanning Unit
Horizon scanning prioritising summary

Volume 14, Number 2:

Dose Verification System for the measurement of radiation dose in patients undergoing radiotherapy for breast and prostate cancer

September 2006

AHTA

Adelaide Health Technology Assessment

[add ISSN]
[add Publications Approval Number]

Electronic copies can be obtained from http://www.horizonscanning.gov.au

Enquiries about the content of this summary should be directed to:

HealthPACT Secretariat
Department of Health and Ageing
MDP 106
GPO Box 9848
Canberra ACT 2606
AUSTRALIA

The production of this *Horizon scanning prioritising summary* was overseen by the Health Policy Advisory Committee on Technology (HealthPACT), a sub-committee of the Medical Services Advisory Committee (MSAC). HealthPACT comprises representatives from health departments in all states and territories, the Australia and New Zealand governments; MSAC and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

This *Horizon scanning prioritising summary* was prepared by Tom Sullivan and Tracy Merlin from the National Horizon Scanning Unit, Adelaide Health Technology Assessment, Discipline of Public Health, Mail Drop 511, University of Adelaide, South Australia, 5005.

PRIORITISING SUMMARY

REGISTER ID: **000227**

NAME OF TECHNOLOGY: **DOSE VERIFICATION SYSTEM**

PURPOSE AND TARGET GROUP: **MEASURING THE RADIATION DOSAGE RECEIVED AT THE TUMOUR SITE IN PATIENTS WITH BREAST OR PROSTATE CANCER**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

- ☒ Yet to emerge
- ☐ Experimental
- ☐ Investigational
- ☐ Nearly established
- ☐ Established
- ☐ Established *but* changed indication or modification of technique
- ☐ Should be taken out of use

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- ☐ Yes ARTG number
- ☒ No
- ☐ Not applicable

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
United States	✓		

IMPACT SUMMARY:

This prioritising summary investigates the value of the Dose Verification System® for improving the precision of radiotherapy in the treatment of breast or prostate cancer.

BACKGROUND

Radiotherapy has become a conventional treatment option for patients with early and late stage cancer. The effectiveness of proton beam radiotherapy has been associated with a number of patient-level factors; including age, comorbidities, and tumour features such as location, size and aggressiveness (Siegelmann-Danieli et al 2006). Successful radiotherapy also depends on accurate radiation delivery. The delivery of radiation according to a pre-specified treatment plan plays an important role in maximising tumour control and minimising damage to healthy tissue (Emami et al 1991). The accurate delivery of radiation has been associated with a number of long-term patient outcomes, including survival and quality of life. In a longitudinal study involving 8 to 12 years of follow-up, Hanks et al (2002) found that an estimated deviation of less than six per cent in the cumulative dosage received by prostate cancer patients resulted in a 65 per cent change in disease free status over time.

In order to ensure accurate radiation delivery, radiation oncologists have relied on a variety of techniques to help visualise tumour location. Techniques such as ultrasound localisation and X-ray based image-guided radiation therapy (IGRT) have emerged as reliable and efficient tools for guaranteeing accurate tumour targeting. A second and equally important requirement in ensuring accurate radiation delivery is the ability to measure the radiation dosage received at the site of the tumour. In addition to ensuring the relevant radiotherapy equipment is calibrated properly (using appropriate phantoms[1]), radiation oncologists have often employed skin surface dosimeters at both entrance and exit sites in order to estimate radiation dosages received at depth (i.e. at the tumour site). Unfortunately, entrance and exit measurements of radiation dosage are easily compromised by factors such as tissue heterogeneity, organ motion, and setup error (Scarantino et al 2004), and as a result, are not strongly predictive of the dosage received at depth.

In 2006, Sicel Technologies Inc. received Food and Drug Administration clearance to market the Dose Verification System® (DVS), a wireless implantable sensor designed to target tumours and measure radiation dosages *in vivo*. At present, the DVS has been approved specifically for the indications of breast and prostate cancer. The DVS consists of four sub-systems; an implantable dosimeter for measuring radiation dosages at depth, an insertion tool for implanting the dosimeter, a reader system for receiving dosage measurements, and finally plan and review software for monitoring daily and cumulative dosage history. The 2mm by 18mm factory calibrated dosimeter uses a MOSFET (metal oxide semiconductor field effect transistor) as the radiation-sensing element and is designed for permanent implantation in the body. The dosimeter is radio-opaque and therefore can be readily visualised by computed tomography during implantation. Once the dosimeter is implanted in the tumour, radiation dosages are communicated telemetrically to the handheld reader system. Each reading takes under ten seconds to be transmitted, and should be obtained both prior to and following individual radiotherapy sessions. Daily and cumulative dosages received at the site of the tumour can then be reviewed using the plan and review software. Since the dosimeter can be viewed using X-rays and ultrasound, it is also functions as a targeting point during radiotherapy.

In addition to possibly improving the quality of radiotherapy treatment delivered at oncology clinics, the DVS may also prove to be useful in a research setting. By offering a more reliable measure of the radiation dosage received at depth, the DVS may be particularly beneficial to research investigating the relationship between delivered dosage and patient response. The DVS could also enable researchers to quantify sources of error, whether systematic or random in nature, that influence the delivery of pre-specified dosages of radiation (Black et al 2006).

CLINICAL NEED AND BURDEN OF DISEASE

In Australia, breast cancer is the most commonly registered type of cancer in women. In 2001, breast cancer was responsible for 29 per cent of new cancer diagnoses in Australia, with

[1] The term phantom can be used to refer to a model, especially a transparent one, of the human body or any of its parts. Phantoms are particularly useful for assessing the precision of measuring equipment. Unlike the human body, in a phantom the underlying quantity of measurement can be assumed to remain constant over successive measurements.

11,791 women in total being diagnosed with the condition. Mortality resulting from breast cancer is also high. In 2001, breast cancer was responsible for a total of 2,594 deaths, making it the leading cause of cancer-related death in Australian women (AIHW & AACR 2004). Similar patterns of incidence and mortality have been documented in New Zealand. Breast cancer was responsible for 28 per cent of new cancer registrations in 2002, with a total of 2,364 New Zealand women being diagnosed with the condition. During 2002, breast cancer also accounted for 17 per cent of total female cancer-related deaths, with a total of 625 women dying from the condition (NZHIS 2006).

After skin cancer, prostate cancer is the most common form of cancer in Australian men. In 2001, prostate cancer was responsible for 23 per cent of new cancer diagnoses, with 11,191 men in total being diagnosed with the disease (AIHW 2005). Although the survival rate of men diagnosed with prostate cancer is favourable compared to many other types of cancer (the five year survival has been estimated to be 83 per cent), prostate cancer is still the second leading cause of cancer-related death in Australian men. In 2001, prostate cancer was responsible for 13 per cent of total male cancer-related deaths, with a total of 2,718 men dying from the disease (AIHW 2004). Like Australia, prostate cancer is a significant health problem in New Zealand. In 2001, 3,046 new prostate cancer registrations were reported in New Zealand, with a total of 592 men dying from the condition that year (NZHIS 2005).

Radiotherapy is a common treatment option for patients diagnosed with breast or prostate cancer. For women with breast cancer, radiotherapy is often used as a secondary treatment following breast conserving surgery or mastectomy (removal of the entire breast). For men diagnosed with prostate cancer, radiotherapy is often used when the risks associated with prostatectomy (surgical removal of the tumour) are too high. Despite being a relatively common mode of treatment, it is somewhat difficult to gauge the exact number of radiotherapy procedures performed on a yearly basis for the specific purposes of treating prostate and breast cancer.

DIFFUSION

The DVS initially received FDA approval for use in breast cancer patients in April 2006. This approval was amended in July 2006 to include the additional indication of prostate cancer. At this stage the DVS has not been marketed in the US, although the company anticipates it will begin taking orders in the third quarter of 2006. It is not known whether the company plans to market the device in Australia.

COMPARATORS

The DVS is the only radiation sensor capable of providing *in vivo* measurements of radiation dosage. In the absence of true *in vivo* measurements, radiation oncologists have typically relied on skin surface dosimeters. The difference in dosages recorded by entrance and exit dosimeters provides an extrapolated estimate of the radiation dosage received at depth. Unfortunately, such an estimate may not necessarily be indicative of the true dosage at depth due to the presence of confounding factors such as tissue heterogeneity, patient motion and setup error (Scarantino et al 2004).

EFFECTIVENESS AND SAFETY ISSUES

Several studies have demonstrated the *in vitro* precision of the DVS. Using an acrylic phantom maintained at body temperature, Briere et al (2005) compared readings from the DVS to the true delivered dosage across a range of practical dosage levels (100 to 400 cGy) (level IV diagnostic evidence). The authors found that readings from the DVS corresponded quite closely to the true delivered dosages, with the standard deviation of the difference ranging between 1.4 and 3.6 per cent of the value of the true dosage. In a similar study, Black et al (2006) compared readings from the DVS (again implanted in an acrylic phantom) to true delivered dosages across a dosage range of 180 to 220 cGy (level IV diagnostic evidence). Again a high level of precision was reported, with the standard deviation of the DVS readings falling within 2 per cent of the true dosage being delivered.

In a clinical pilot study addressing the safety and effectiveness of the DVS, Scarantino et al (2005) implanted the device in ten patients with biopsy proven malignant tumours (level IV diagnostic evidence). Each patient recruited in the study was due to receive at least four weeks of radiotherapy with a minimum daily dosage in the range of 150 to 300 cGy. Following implantation of the device, all patients underwent computed tomography simulation in the treatment position in order to identify the exact location of the DVS. Computed tomography was then repeated two and four weeks later in order to assess movement of the device. Over the four-week investigation period, migration of the sensor from the point of initial placement was discovered in only one of the ten patients (due to implantation in unconsolidated tissue). The patients reported no adverse events during implantation of the device or over the follow-up period. In terms of the performance of the DVS, the difference between the expected dosage and the dosage measured at depth exceeded 8 per cent in magnitude on almost 50 per cent of occasions. Taking into account previous research demonstrating the *in vitro* precision of the DVS, the results suggest that the influence of confounding factors (such as organ motion, tissue heterogeneity etc) on the delivery of radiation is extensive.

In addition to evaluating the *in vitro* precision of the DVS, Black et al (2006) investigated *in vivo* performance by implanting the device in the gross tumour volume or the collateral normal tissue of 18 patients with biopsy proven malignancies (level IV diagnostic evidence). During the course of the study, a total of 861 individual dosage measurements were relayed by the implantable dosimeter. Results indicated that the difference between the expected dosage and the dosage measured at depth exceeded five per cent in magnitude on at least 40 per cent of all treatment sessions for 12 of the 18 patients. Again the results highlight the problematic influences of organ motion, tissue heterogeneity and setup error on the accurate delivery of radiation at the site of the tumour.

COST IMPACT

Sicel Technologies Inc. is yet to disclose the price of the DVS. The introduction of the DVS is unlikely to be associated with any additional costs however, as most oncology practices already have the equipment required to visualise the device.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified/raised in the sources examined.

OTHER ISSUES

Dr. Charles Scarantino, an author on several of the clinical studies into the effectiveness of the DVS, is the principal founder and current chairman of Sicel Technologies Inc.

Results from early clinical trials with the DVS have led authors to believe that the use of two sensors, rather than one, may be preferable for the purpose of understanding and quantifying sources of variation in the dosage received at depth (see for example Black et al 2006). Two independent measures of *in vivo* dosage may facilitate the decomposition of total dosage error (the difference between expected and measured dosage) into measurement error (due to imprecision of the sensors) and error resulting from factors such as tissue heterogeneity, organ motion and setup error.

CONCLUSION:

Early studies have demonstrated that the DVS is a useful device for quantifying dosages at the site of the tumour. The ability of the DVS to monitor deviations between intended dosage and dosage received at depth suggests that the device may play an important quality assurance role in the delivery of radiotherapy. The device also offers promise for gaining a better understanding of the factors responsible for fluctuations in the dosage received at depth. Despite this, evidence regarding the safety and effectiveness of the DVS is limited. Without a gold standard for measuring dosage at depth, further studies involving the implantation of multiple sensors are required to demonstrate the long-term reliability and precision of the device.

HEALTHPACT ACTION:

Although evidence is limited regarding the effectiveness of the DVS, the technology may play an important role in radiotherapy quality assurance. It is therefore recommended that the technology be monitored.

SOURCES OF FURTHER INFORMATION:

AIHW (2004). *Cancer in Australia 2001,* Australian Institute of Health and Welfare, Canberra.

AIHW (2005). *Cancer incident projections Australia 2002 - 2011,* Austrlalian Institute of Health and Welfare, Canberra.

AIHW and AACR (2004). *Cancer in Australia 2001,* Australian Institute of Health and Welfare (AIHW) and Australasian Association of Cancer Registries (AACR), Canberra.

Black, R. D., Scarantino, C. W. et al (2006). 'An analysis of an implantable dosimeter system for external beam therapy', *Int J Radiat Oncol Biol Phys,* accepted for publication 2006.

Briere, T. M., Beddar, A. S. & Gillin, M. T. (2005). 'Evaluation of precalibrated implantable MOSFET radiation dosimeters for megavoltage photon beams', *Med Phys,* 32 (11), 3346-3349.

Emami, B., Lyman, J. et al (1991). 'Tolerance of normal tissue to therapeutic irradiation', *Int J Radiat Oncol Biol Phys,* 21 (1), 109-122.

Hanks, G. E., Hanlon, A. L. et al (2002). 'Dose response in prostate cancer with 8-12 years' follow-up', *Int J Radiat Oncol Biol Phys,* 54 (2), 427-435.

NZHIS (2005). *Cancer: New Registrations and Deaths 2001,* New Zealand Health Information Service, Wellington.

NZHIS (2006). *Cancer: New Registrations and Deaths 2002,* New Zealand Health Information Service, Wellington.

Scarantino, C. W., Rini, C. J. et al (2005). 'Initial clinical results of an in vivo dosimeter during external beam radiation therapy', *Int J Radiat Oncol Biol Phys,* 62 (2), 606-613.

Scarantino, C. W., Ruslander, D. M. et al (2004). 'An implantable radiation dosimeter for use in external beam radiation therapy', *Med Phys,* 31 (9), 2658-2671.

Siegelmann-Danieli, N., Khandelwal, V. et al (2006). 'Breast cancer in elderly women: outcome as affected by age, tumor features, comorbidities, and treatment approach', *Clin Breast Cancer,* 7 (1), 59-66.

LIST OF STUDIES INCLUDED

Total number of studies	
Level IV Diagnostic evidence	3

SEARCH CRITERIA TO BE USED:

Radiotherapy Dosage

Radiometry/adverse effects/*instrumentation/methods

Telemetry/adverse effects/*instrumentation/methods

Dose-Response Relationship, Radiation