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Horizon Scanning Technology

Prioritising Summary

TomoTherapy HI-ART System Radiotherapy planning and treatment for cancer patients

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PRIORITISING SUMMARY (UPDATE 2009)

REGISTER ID:	**000180**
NAME OF TECHNOLOGY:	**TOMOTHERAPY HI-ART SYSTEM®**
PURPOSE AND TARGET GROUP:	**RADIOTHERAPY PLANNING AND TREATMENT FOR CANCER PATIENTS**

2009 EFFECTIVENESS AND SAFETY ISSUES:

A significant amount of literature has been published on tomotherapy since the preparation of the original prioritising summary in December 2005. Most of the published studies focused on comparisons between tomotherapy and standard cancer radiotherapy, dose optimisation and toxicity assessment, or experimental treatment of cancer patients. Tomotherapy has been used as a therapy for a wide variety of cancer types.

Moon et.al (2009) investigated the ability of four external beam cancer therapies to deliver the desired radiation dose to the target tissue whilst limiting the radiation dose delivered to the surrounding normal tissue. The population in the study consisted of 30 patients who had undergone lumpectomy for early stage breast cancer. This study only modelled planning with the therapies; patients were not assigned to actual therapies. The patients were imaged for planning with a CT scan. The four therapies assessed were three-dimensional conformal radiation therapy (3D-CRT), intensity-modulated radiation therapy (IMRT), helical tomotherapy (TOMO), and proton beam therapy (PBT). Treatment plans were designed for each patient using all of the four techniques. The treatment plans were then assessed for coverage of the desired target and the undesired irradiation of healthy tissue or sensitive organs (for example heart or lungs). The overall conclusion of the authors was that all techniques showed acceptable dosage to both the target tissue and surrounding normal tissue. There were some significant differences between the techniques with PBT showing the most accurate dose profile with the highest dose delivered to the target site and the least dose to ipsilateral breast tissues. This was followed by TOMO, IMRT, and 3D-CRT respectively. TOMO plans exposed both heart and lungs to above permissible levels of irradiation and this was significantly more than the other three techniques (Moon et al 2009) (Level IV intervention evidence).

A second planning evaluation study also investigated four radiotherapy techniques for breast cancer therapy. The four techniques in the study were interstitial brachytherapy (IB), 3D-CRT, supine TOMO and prone TOMO. Results are shown in Table 1. The authors conclude that IB and prone TOMO confer the best tissue sparing treatment (Patel et al 2007) (Level IV intervention evidence).

Table 1 Comparison of four irradiation therapy planning outcomes

Irradiation technique	Average % of Target receiving 90% dose	Average % of Target receiving 100% dose	Average % of ipsilateral breast receiving the 100% dose	Average % of ipsilateral breast receiving the 50% dose	Ipsilateral lung dose (Gy)	Heart dose (Gy)
IB	98.4%	96.1%	12%	24%	1.3 Gy_3 (0.6 to 2.6)	0.7 Gy_3 (0.3–2.5)
3D-CRT	99.9%	92.3%	26%	52%	3.7 Gy_3 (1.0 to 7.1)	0.5 Gy_3 (0.0 –2.9)
Supine TOMO	99.3%	95.2%	18%	47%	3.3 Gy_3 (0.7 to 5.5)	1.2 Gy_3 (0.8 –3.3)
Prone TOMO	99.8%	95.4%	15%	43%	1.2 Gy_3 (0.1 to 4.3)	0.8 Gy_3 (0.1–2.4)

Another planning comparison investigated strategies based on tomotherapy and 3D-CRT treatments for 10 high-risk prostate cancer patients. Three TOMO targeting profiles were assessed: target, target + lymph nodes, and target + lymph nodes + soft tissues. These were compared against the control treatment 3D-CRT. Overall the three TOMO strategies were significantly better at sparing critical organs from irradiation. The TOMO strategy directed at target + lymph nodes + soft tissues was found to be best at delivering target, lymph node and pelvic tissue dose at a cost of a slightly higher dose to critical organs (Yuen et al 2008) (Level IV intervention evidence).

Several other planning studies found TOMO to be equal to or better than standard cancer irradiation treatments with respect to target dosage and normal tissue sparing (Bauman et al 2007; Jhaveri et al 2009; Kim et al 2009; Rochet et al 2008) (Level IV intervention evidence).

TOMO (n=55) was compared to Linear Accelerator based therapy (n=43) in 98 patients with prostate cancer. The primary outcome was acute radiation toxicity. During the therapy planning stages it was noted that TOMO plans required fine tuning to avoid increased dosage to the skin and abdomen. After treatment patients were monitored for acute toxicity symptoms. The authors found that TOMO gave a reduced acute gastrointestinal (GI) toxicity yet increased acute genitourinary (GU) toxicity. They speculated that this was due to different distributions of radiation doses across different tissues (Keiler et al 2007) (Level III-2 intervention evidence)..

The toxicity of TOMO was investigated by several groups with all concluding the acute toxicity of TOMO was either less than conventional therapy or within the expected range due to the radiation delivered (De Ridder et al 2008; Di Muzio et al 2009; Ramsey et al 2007; Wong et al 2009) (Level IV intervention evidence).

A case series of 150 patients was reported on in a treatment planning study by Sterzing et al with no clinical results presented. A wide variety of cancer types were treated with TOMO as detailed in Table 2. Megavoltage CT was used to plan the patient's therapies daily before treatment. The authors concluded that routine TOMO is easy to incorporate into a normal treatment centre within a short period of time. Although no clinical data was presented to support this claim, the authors report TOMO to be excellent for the treatment of standard cases and in addition allowed

treatment of complex cases that normally would not be able to be treated with radiotherapy. Patients who were restricted by obesity, pain, immobilisation, or phobia were also able to be treated with TOMO (Sterzing et al 2008) (Level IV intervention evidence).

Table 2 Tomotherapy cancer treatment

Radiotherapy site	Cancer type
Central nervous system (n = 7)	Prostate cancer (n = 28)
Head and neck (n = 28)	Breast cancer (n = 17)
Thoracic (n = 37)	Gastrointestinal tumours (n = 19)
Abdominal (n = 58)	Pharyngeal carcinoma (n = 14)
Skeletal system (n = 20)	Lymphoma (n = 13)
	Metastatic disease (bone n = 14, liver n = 6, lung n = 4, lymph node n = 2)
	Sarcoma (n = 8)
	Malignant pleural mesothelioma (n = 5)
	Ovarian cancer treated with whole abdominal irradiation (n = 4)
	Lung cancer (n = 3)
	Skin malignancies (n = 3)
	Chordoma (n = 2)
	Meningioma (n = 2)
	One ependymoma and one medulloblastoma treated with craniospinal axis irradiation (n = 2)
	Others (n = 4)

Tomotherapy is still an experimental cancer therapy with most reports either focusing on planning models, acute toxicity or dose optimisation. Tomotherapy is often referenced against standard cancer radiation therapies such as 3D-CRT. Planning studies have found tomotherapy to be, in general, superior to standard techniques. One exception was the superiority of proton beam therapy over tomotherapy. Long term outcomes and randomised clinical trials are needed to assess the true effectiveness of this therapy.

2009 COST IMPACT:

No cost effectiveness data was found during the preparation of this update.

2009 SUMMARY OF FINDINGS

Tomotherapy has been used for a very wide range of cancer types including some normally refractory to standard radiation therapy. Most studies reviewed were either tomotherapy plan modelling, assessments of tomotherapy acute toxicity, or case series of tomotherapy treatments. In general all reports of tomotherapy are generally favourable with usually better than standard therapy outcomes. Despite this, no high quality, long-term evidence was found on effectiveness of tomotherapy, so it remains to be seen whether tomotherapy improves clinical outcomes such as survival time, or

symptom reduction. No cost effectiveness data were found preventing comparisons with existing therapies.

HEALTHPACT ACTION:

The large amount of literature generated on tomotherapy is generally positive yet of low quality. Controlled trials comparing tomotherapy to standard techniques are needed before further investigation of this subject is warranted. It is likely that this technology will emerge in the long-term and if high quality research is published in this field it will be identified by routine horizon scanning. Therefore HealthPACT have recommended that no further assessment is warranted.

LIST OF STUDIES INCLUDED

Total number of studies	
Level III-2 intervention evidence	1
Level IV intervention evidence	12

SOURCES OF FURTHER INFORMATION:

Bauman, G., Yartsev, S. et al (2007). 'A prospective evaluation of helical tomotherapy', *Int J Radiat Oncol Biol Phys,* 68 (2), 632-641.

De Ridder, M., Tournel, K. et al (2008). 'Phase II study of preoperative helical tomotherapy for rectal cancer', *Int J Radiat Oncol Biol Phys,* 70 (3), 728-734.

Di Muzio, N., Fiorino, C. et al (2009). 'Phase I-II study of hypofractionated simultaneous integrated boost with tomotherapy for prostate cancer', *Int J Radiat Oncol Biol Phys,* 74 (2), 392-398.

Jhaveri, P. M., Teh, B. S. et al (2009). 'Helical Tomotherapy Significantly Reduces Dose to Normal Tissues When Compared to 3D-CRT for Locally Advanced Rectal Cancer', *Technol Cancer Res Treat,* 8 (5), 379-386.

Keiler, L., Dobbins, D. et al (2007). 'Tomotherapy for prostate adenocarcinoma: a report on acute toxicity', *Radiother Oncol,* 84 (2), 171-176.

Kim, Y. B., Kim, J. H. et al (2009). 'Dosimetric Comparisons of Three-dimensional Conformal Radiotherapy, Intensity-Modulated Radiotherapy, and Helical Tomotherapy in Whole Abdominopelvic Radiotherapy for Gynecologic Malignancy', *Technol Cancer Res Treat,* 8 (5), 369-378.

Moon, S. H., Shin, K. H. et al (2009). 'Dosimetric comparison of four different external beam partial breast irradiation techniques: three-dimensional conformal radiotherapy, intensity-modulated radiotherapy, helical tomotherapy, and proton beam therapy', *Radiother Oncol,* 90 (1), 66-73.

Patel, R. R., Becker, S. J. et al (2007). 'A dosimetric comparison of accelerated partial breast irradiation techniques: multicatheter interstitial brachytherapy, three-dimensional conformal radiotherapy, and supine versus prone helical tomotherapy', *Int J Radiat Oncol Biol Phys,* 68 (3), 935-942.

Ramsey, C. R., Scaperoth, D. et al (2007). 'Image-guided helical tomotherapy for localized prostate cancer: technique and initial clinical observations', *J Appl Clin Med Phys,* 8 (3), 2320.

Rochet, N., Sterzing, F. et al (2008). 'Helical tomotherapy as a new treatment technique for whole abdominal irradiation', *Strahlenther Onkol*, 184 (3), 145-149.

Sterzing, F., Schubert, K. et al (2008). 'Helical tomotherapy. Experiences of the first 150 patients in Heidelberg', *Strahlenther Onkol*, 184 (1), 8-14.

Wong, J. Y., Rosenthal, J. et al (2009). 'Image-guided total-marrow irradiation using helical tomotherapy in patients with multiple myeloma and acute leukemia undergoing hematopoietic cell transplantation', *Int J Radiat Oncol Biol Phys*, 73 (1), 273-279.

Yuen, J., Rodrigues, G. et al (2008). 'Comparing two strategies of dynamic intensity modulated radiation therapy (dIMRT) with 3-dimensional conformal radiation therapy (3DCRT) in the hypofractionated treatment of high-risk prostate cancer', *Radiat Oncol*, 3, 1.

PRIORITISING SUMMARY (2005)

REGISTER ID: **000180**

NAME OF TECHNOLOGY: **TOMOTHERAPY HI-ART SYSTEM®**

PURPOSE AND TARGET GROUP: **RADIOTHERAPY PLANNING AND TREATMENT FOR CANCER PATIENTS**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

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

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☐	Yes	ARTG number
☒	No	
☐	Not applicable	

The TomoTherapy HI-ART System® received FDA approval in the United States in November 2003.

INTERNATIONAL UTILISATION:

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

IMPACT SUMMARY:

TomoTherapy Inc. provides the TomoTherapy HI-ART System® for radiotherapy planning and treatment of cancer.

BACKGROUND

Standard radiation therapy in cancer patients uses high energy X-rays to damage the DNA in cancer cells and is delivered over a number of weeks. Radiation therapy is a localised therapeutic approach which aims to deliver a high radiation dose to the tumour, while minimising the radiation dose, and therefore damage, to the surrounding normal tissue. A typical course of radiation treatment may extend over several weeks, during which time a patient's organ volume and location may change. Changes in tumour size and location may affect the position of the radiation target

area, resulting in irradiation and damage of normal tissue. In addition, radiation misalignment may result in under-treatment of the tumour.

Tomotherapy addresses the limitations of standard radiation therapy as it allows the physician to accurately visualise target areas so that position adjustments can be made just prior to treatment. Tomotherapy delivers an advanced form of intensity modulated radiation therapy (IMRT). IMRT is a cancer treatment modality that uses angles and radiation beam shapes to treat tumours and involves changing the size, shape and intensity of the radiation
beam during treatment to conform to a patient's tumour, while sparing the surrounding healthy tissue (TomoTherapy Inc.). The interest in tomotherapy is in its enhanced precision (compared to conventional IMRT) in accurately distributing the radiation dose while delivering less radiation to the surrounding healthy tissue and altering radiation dose to compensate for patient movement—reducing side effects experienced by patients.

The Tomotherapy HI-ART System® is the first device to provide 3-D computerised tomography (CT) imaging immediately prior to treatment to verify the location of a patient's tumour, allowing for changes in tumour size and location. The TomoTherapy System® can record the dose and location of the radiation given to a patient, providing physicians a record of the previous session, and to accommodate adjustments as required.

The TomoTherapy HI-ART System® is intended to be used as an integrated system for the planning and delivery of IMRT for the treatment of cancer. During treatment, the patient moves through the TomoTherapy machine on a couch platform while radiation is delivered to the tumour site in a 360 degree helical (spiral) pattern. While conventional radiotherapy delivers a wide beam of radiation from just a few directions, the TomoTherapy system can deliver small beams of radiation from every point on a spiral (Figure 1). The system consists of a linear accelerator mounted on a ring gantry, which moves in unison with a multileaf collimator (MLC).

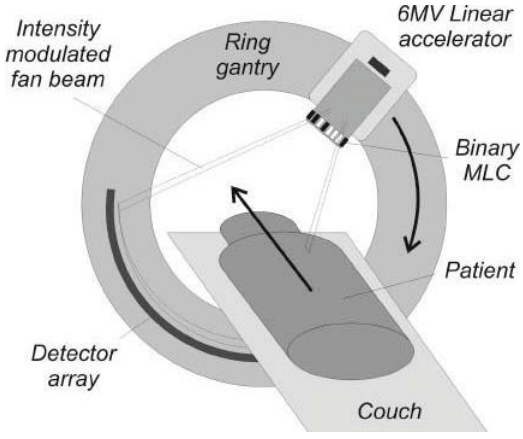

Figure 1. Schematic drawing of helical tomotherapy unit (Kron et al 2005)

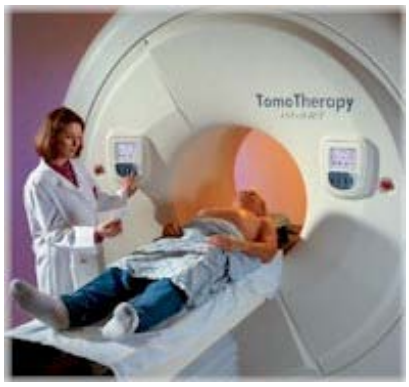

Figure 2 Hi-Art Tomotherapy unit Printed with permission

The computer-controlled MLC has two sets of interlaced leaves that move in and out rapidly, constantly modulating the radiation beam as it leaves the accelerator. The patient couch moves simultaneously, guiding the patient slowly through the centre of

the gantry. With each rotation of the linear accelerator, the radiation beam is directed at a slightly different plane, irradiating a different section of the tumour (Figure 2).

CLINICAL NEED AND BURDEN OF DISEASE

Tomotherapy may be applied to a range of cancers including breast, lung and prostate. In Australia during the year 2000, incidence rates for all cancers were 536 and 390 per 100,000 for males and females, respectively. The corresponding mortality rates for the same period were 245 and 148 per 100, 000, for males and females, respectively (AIHW & AACR 2003). A recent health survey in New Zealand reported that 1 in 20 adults (5% of the population) had ever been diagnosed with a cancer (Ministry of Health 2004).

DIFFUSION

The HI-ART System® was first used in 2002 in Canada. There are currently 30 TomoTherapy installations world wide. There are currently no Hi-ART Systems installed in Australia.

COMPARATORS

Several imaging techniques are employed for radiation therapy planning and external treatment for cancer patients. Typically a patient will receive high radiation doses of 60-70 Gy, given in 30 to 40 daily fractions at the rate of 5 fractions per week (van Dyke et al 2002). Imaging modalities include: 3-D imaging using CT, magnetic resonance imaging (MRI), single photon emission tomography (SPECT), or positron emission tomography (PET). For radiation dose delivery linear accelerators, generating electron energies between 4 and 25 MeV, are generally used for producing x-ray beams for the treatment of tumours.

Brachytherapy is a treatment option that involves *internal* delivery of radiation by the use of radioactive implants that deliver high radiation doses to specific cancer cells, without damaging adjacent normal tissues. Brachytherapy is often used in addition to external beam irradiation in the treatment of patients with prostate, breast, head and neck cancer.

An alternative treatment for internal radiation delivery is the use monoclonal antibodies, which target tumour antigens. Radioactive substances my be attached to monoclonal antibodies, which in turn target tumour antigens, delivering radiation while sparing normal tissue.

2005 EFFECTIVENESS AND SAFETY ISSUES

At the time of preparing this summary there were limited studies which described clinical planning[1] of tomotherapy or compared tomotherapy planning to conventional radiotherapy treatment planning or other IMRT technologies for lung and brain cancer

[1] Planning of tomotherapy involves a complex series of steps which generates individualised patient radiation therapy planning data. Planning takes into account the size and position of the tumour, as well as other organs at risk of radiation exposure. This data is transferred to the tomotherapy treatment planning computer. An optimised treatment planned is then developed, which provides inverse planning capabilities, radiation dose, radiation exposure time and determines the leaf positions for all gantry angles and couch positions. This data are then transferred to the tomotherapy treatment unit for patient delivery.

(Kron et al 2004, Yartsev et al 2005). Two case studies were identified reporting on its use for breast and brain cancer (Hui et al 2004 abstract only, Bauman et al 2005). There were no studies that compared clinical use of tomotherapy to other radiotherapy modalities.

One low quality study (level III-3 intervention evidence) compared the results of tomotherapy *treatment planning*, for 12 patients with brain tumours, to previous planning results for five other radiation therapy techniques (Yartsev et al 2005). The study examined in particular the theoretical performance of the techniques in avoiding radiation to organs at risk in close proximity to the tumours. All radiation treatment modalities were programmed into planning software that calculated planning target volumes of the tumours to radiate (maximum radiation dose) and other organs at risk (minimised radiation dose). When data were entered into the computer program for each patient for all radiotherapy modalities tomotherapy demonstrated significantly better minimum target dose coverage than three other radiotherapy techniques and was as effective as photon methods ($p<0.05$). It should be stressed that this study provided planning data only, and that patients did not undergo tomotherapy treatment.

In a separate study (level III-3 intervention evidence) tomotherapy plans were developed for 15 patients with stage III inoperable lung cancer, which were then compared to IMRT planning. The quality of tomotherapy planning correlated well (accurately targeted tumour area with high dose radiation and avoided irradiating organs at risk), or was slightly improved, compared to IMRT planning (Kron et al 2004).

2005 Cost Impact

It is not possible to estimate at this stage the likely cost impact of establishing tomotherapy in clinical practice as there are no available data on cost effectiveness. It is not known whether the use of tomotherapy would result in the need for less and/or shorter treatment sessions for cancer patients as this has not been studied to date. The estimated cost of the Hi-Art® system is between $AUD 5.3-5.5 million (personal communication, Australian distributor).

Ethical, Cultural or Religious Considerations

No issues were identified/raised in the sources examined.

2005 Other Issues

An internet search for tomotherapy at the time of preparing this summary revealed several ongoing clinical trials of tomotherapy for different cancers in the United States and United Kingdom. Presentations on the use of tomotherapy for the treatment of prostate cancer will be delivered at an international conference to be held in Wollongong (5-8th December, 2005) (Micro- and Mini-Dosimetry & International Prostate Cancer Treatment).

2005 Conclusion:

There is limited clinical evidence available to date describing the use of tomotherapy either in Australia or overseas. However, it is currently being investigated in clinical trials worldwide.

2005 HEALTHPACT ACTION:

Tomotherapy is not funded under the Medicare Benefits schedule. However, given the high level of interest in the potential for tomotherapy, in conjunction with the current lack of clinical evidence, it is recommended that this technology be monitored.

2005 SOURCES OF FURTHER INFORMATION:

AIHW & AACR (2003). Cancer in Australia 2000. AIHW cat no CAN 18, Australian Institute of Health and Welfare (AIHW) and Australasian Association of Cancer Registries (AACR), Canberra.

Bauman, G., Yartsev, S. et al (2005). 'Helical tomotherapy for craniospinal radiation', *Br J Radiol*, 78 (930), 548-552.

Beavis, A. W. (2004). 'Is tomotherapy the future of IMRT?' *Br J Radiol*, 77 (916), 285-295.

Food and Drug Administration (2005). *k042739* [Internet]. Food and Drug Administration. Available from: http://www.fda.gov/cdrh/pdf4/k042739.pdf [Accessed 16th November].

Hui, S. K., Das, R. K. et al (2004). 'Helical tomotherapy as a means of delivering accelerated partial breast irradiation', *Technol Cancer Res Treat*, 3 (6), 639-646.

Kron et al (2005). *Helical Tomotherapy – a combined approach to intensity modulated and adaptive radiotherapy*. [Internet]. Paper presented at AMPICON 2005, International conference on Medical Physics & Radiation safety , 26th Annual Conference of Association of Medical Physicists of India (AMPI),November 10, 11 & 12, 2005. Available from: http://www.ampicon2005.org/PDF_Version/I3_Tomas_kron.pdf [Accessed 16th November 2005].

Kron, T., Grigorov, G. et al (2004). 'Planning evaluation of radiotherapy for complex lung cancer cases using helical tomotherapy', *Phys Med Biol*, 49 (16), 3675-3690.

Ministry of Health (2004). *A Portrait of Health: Key results of the 2002/03 New Zealand Health Survey*. Wellington: Ministry of Health.

TomoTherapy Inc. (2005). *TomoTherapy*. [Internet]. Available from: http://www.tomotherapy.com/patient/whatistomo.html [Accessed 16th November 2005]

Van Dyk, J. et al (2002). 'Tomotherapy: A "revolution" in radiation therapy' *Physics in Canada* 3/4, 79-86.

Welsh, J. S., Patel, R. R. et al (2002). 'Helical tomotherapy: an innovative technology and approach to radiation therapy', *Technol Cancer Res Treat*, 1 (4), 311-316.

Yartsev, S., Kron, T. et al (2005). 'Tomotherapy planning of small brain tumours', *Radiother Oncol*, 74 (1), 49-52.

LIST OF STUDIES INCLUDED

Total number of studies	
Level III interventionevidence	2

SEARCH CRITERIA TO BE USED:

Neoplasms/ radiotherapy/ therapy

Radiotherapy Dosage
Radiotherapy Planning, Computer-Assisted
Radiotherapy, Conformal/ methods
Tomography, X-Ray Computed