NICE advice

AlignRT for intracranial stereotactic radiosurgery

Medtech innovation briefing
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Summary

- The **technology** and indication described in this briefing is the AlignRT patient position monitoring system, for guiding intracranial stereotactic radiosurgery (SRS). This may avoid incomplete or inaccurate treatment that can be caused by patient movement.
- The **innovative aspects** are that it does not use potentially uncomfortable patient frames or bite plates, additional ionising radiation, or separate radiation sources or tracking systems.
- The intended **place in therapy** would be in a standard radiation treatment suite with a linear accelerator (LINAC). It would be used in people with secondary brain tumours as an adjunct to existing position monitoring systems. These existing systems use X-rays or CT scanning and radiologist/radiographer visual monitoring.
- The **main points from the evidence** summarised in this briefing are from 5 observational and retrospective studies including a total of 244 adult patients in a tertiary care setting in the US. They suggest that AlignRT is as effective as existing position monitoring systems for people having SRS to treat brain tumours.

- **Key uncertainties** are that the evidence is limited in quality and quantity. There are no direct comparisons of AlignRT with current NHS comparators for position monitoring, although such trials are unusual in this clinical area.
- The **cost** of AlignRT is £250,000 per unit (excluding VAT) plus an annual service charge of £25,000 or an additional estimated cost per procedure of £1,000 per patient treatment. Savings that could be offset against this include more accurate initial treatment and a reduced need for repeat treatments, or management of the adverse effects of increased radiation exposure.

The technology

AlignRT (Vision RT) is a system for monitoring the position and movement of a person during set-up for, and treatment with, stereotactic radiosurgery (SRS). SRS and stereotactic radiotherapy (SRT) are accurate forms of radiation treatment that can be used to treat small secondary brain tumours. SRT delivers the radiation in a number of daily doses, called fractions. In SRS, the radiation is delivered in a single fraction.

AlignRT uses 3 video cameras to monitor the person's position with accuracy to within 1 mm or 1-degree rotation during radiotherapy. AlignRT communicates with the linear accelerator (LINAC) delivering the radiation, and instructs it to stop the radiation beam if the person moves. This prevents radiation from being delivered to neighbouring tissue and organs, which can lead to unwanted side effects and incomplete treatment of the target tumour. AlignRT can also be used in the treatment of other cancers, but these are beyond the scope of this briefing.

AlignRT consists of 3 wall- or ceiling-mounted video camera projector pods, each including a red-light surface projector. During use, the person lies with their head in a custom-made head support to minimise movement. Visible red light in a random pattern is projected from each camera pod onto the person's head, and the resultant light is detected by 2 sensors in each pod. The AlignRT software generates a real-time 3D surface image of the person. This real-time image is aligned with an image of the bony anatomy of the person's head that has been taken from an earlier CT scan, which is done to image the tumour and its location to plan treatment. By aligning the real-time and treatment-planning images, clinicians can predict the tumour location.

If needed, the person's position can be adjusted using the AlignRT interface with the automatic treatment couch control system. Internal imaging is performed using the linear

accelerator to confirm the tumour location and SRS treatment can then begin.

If AlignRT detects any movement during treatment it instructs the linear accelerator to stop the radiation beam, or prompt the users to manually stop treatment. This allows the person to be moved back into the correct position before treatment can start again.

AlignRT integrates with the radiotherapy system. It is also marketed as part of the Varian EDGE radiosurgery system (Varian Medical Systems), when it is called the optical surface monitoring system (OSMS).

Innovations

AlignRT uses video cameras to track movement during treatment, as an alternative to more invasive and potentially positioning systems such as bite plates, or external fixation devices such as full-face masks or frames, which may need to be surgically placed using screws or pins. In addition, AlignRT uses a custom-made head support which, unlike some other devices, does not cover the face, and is designed to be more comfortable and reduce anxiety and feelings of claustrophobia. AlignRT also allows the person to be monitored throughout the treatment, which may not be possible with other positioning techniques.

Using AlignRT allows treatment-planning CT scans to be done and the custom head support to be made several days before treatment. In monitoring systems that use a surgically fixed external frame, the whole treatment cycle of dosimetry planning, clinical treatment planning, sign off and treatment has to be completed within 1 session once the frame is in place. This is because alignment to the CT scans is lost once the frame is removed, and treatment planning would have to be repeated. This can place pressure on the staff and treatment suite workflow, as well as being distressing and time-consuming for the person being treated. Because AlignRT can be used over several sessions using the same head support, it can be used for SRT as well as SRS.

Current NHS pathway

Microsurgery, with or without whole-brain radiotherapy, is usually offered for large tumours in accessible positions in the brain.

People in whom SRS or SRT are suitable are defined in the NHS England's clinical

commissioning policy on stereotactic radiosurgery as having good performance status, controllable systemic disease and low-volume metastatic disease. SRS can be considered in a small subset of patients when there is evidence of its effectiveness, and when conventional surgery is contraindicated or the risk of functional disability would be increased through surgery. Treatment is planned for each person by a multidisciplinary team. AlignRT would be used as part of delivering SRS or SRT for people who are suitable for this treatment.

Current methods of positioning involve the standard radiotherapy-planning CT scan and subsequent patient alignment using X-ray imaging in several planes and adjustment of the patient couch. The patient's head is held in position using an appropriate method. Other systems such as Exactrac, CyberKnife and Gamma Knife use dedicated X-ray or additional radiation sources.

The AlignRT system is used in the NHS for guiding breast cancer radiosurgery.

NICE is aware of the following CE-marked devices that appear to fulfil a similar function to AlignRT:

- Catalyst (C-Rad) – uses a similar optical system to position the person.
- Bite-block (Zmed/Varian) – uses infrared tracking; the person must hold a reflective unit between their teeth.
- Exactrac (Brainlab) – uses X-ray tracking.
- Gamma Knife (Elekta) – uses X-ray tracking; the Gamma Knife dedicated system must be installed for it to be used. This system also needs a head-frame screwed to the person's skull, or additional integrated stereotactic cone beam CT for it to be used as a mask system.
- CyberKnife (Accuray) – uses X-ray; the CyberKnife dedicated system must be installed.

Population, setting and intended user

AlignRT would be used in patients with brain tumours in whom SRS is suitable. SRS would be done in specialist tertiary centres with linear accelerator (LINAC) facilities. It would be used by a trained therapy radiographer.

Costs

The list price of AlignRT is £250,000 (excluding VAT). The annual service charge is £25,000. Assuming a 10-year lifespan, the total cost of ownership would be £50,000 per year. If 50 people were treated for brain tumours per year, the cost of AlignRT would be £1,000 per treatment.

AlignRT can also be used while treating other more common cancers, including breast cancer. If purchased by a centre that used it to treat a range of cancers, then this may reduce the cost per treatment proportionally. Other indications are outside the scope of this briefing.

Training is provided by the company and is included in the cost of AlignRT. Training consists of 2.5 days of training at the company's office for a therapeutic radiographer and physicist, with the intention that these 2 staff then train the rest of the department. A representative from the company then visits the site for 2 days to put the device into use.

Costs of standard care

The company estimates that the cost of comparable technologies (including installation) would be £600,000 to £3 million, depending on the choice of system. Annual service charges would range from £50,000 to £250,000 per year.

Based on the company's assumptions of comparator lifespan and throughput, this would equate to at least £2,200 per treatment.

Resource consequences

Adopting AlignRT is not expected to have any resource consequences, beyond the cost of the equipment, or to need any changes in facilities or infrastructure. The company has stated AlignRT is compatible with all common LINAC systems used in the UK.

If the same number or more people are treated in daily schedules as they are now, using AlignRT could improve workflows at an SRS/SRT unit. AlignRT can allow the treatment of multiple brain tumours in a single treatment plan, potentially reducing treatment time. This capability is not available with some other devices. AlignRT can be used with existing treatment technologies and treatment-planning software, unlike some other solutions that

need a new treatment-planning platform to be commissioned and training on it provided. The technology is only likely to provide the savings in circumstances where investment in new or replacement systems are being contemplated, because of the high upfront costs of procuring the technology.

Regulatory information

AlignRT was CE marked as a class IIb device in June 2016.

The Medicines and Healthcare products Regulatory Agency (MHRA) has issued the following manufacturer field safety notices or medical device alerts for this technology:

- 2014/010/020/601/005 (Vision RT reference: 3010769039-15/10/14-001-C). This relates to an issue with the MMI interface (now resolved).
- 2014/011/018/601/001 (Vision RT reference: 3010769039-051114-001-C). This relates to an issue with the AlignRT key-switch (now resolved).
- 2015/011/018/601/010 (Vision RT reference: 3010769039-11/16/15-001-C). This was resolved in March 2017.
- 2016/007/001/601/008 (Vision RT reference: 3010769039-062416-001-C). This was resolved in March 2017.

After the first 2 alerts, a product upgrade was released and installed on all affected devices and the field safety corrective actions are now closed.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

No specific equality issues were identified but all patients with cancer are considered disabled from the point of diagnosis. The use of AlignRT would allow people who could not hold a bite-block to access therapy more easily, and would provide benefits to patients who suffer from anxiety or claustrophobia in a closed-face mask.

Clinical and technical evidence

A literature search was carried out for this briefing in line with the interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Five studies are summarised in this briefing, with a reported total of 259 patients. Table 1 summarises the clinical evidence as well as its strengths and limitations.

Overall assessment of the evidence

The evidence for AlignRT is limited to small studies and retrospective analyses of patient records. This quantity and quality of evidence is typical for this clinical area because intracranial tumours of all types are relatively rare.

There is a degree of overlap between the patient cohorts reported in some of the studies, so the total number of patients in these studies is not clear. All of the studies were completed in the US and the generalisability of these studies to NHS practice is not clear.

The evidence shows that AlignRT can accurately position a patient for radiosurgery at a similar level of accuracy to existing methods such CT- and frame-based methods.

Table 1 summarises the clinical evidence as well as its strengths and limitations.

Table 1 Summary of selected studies

Pham et al. (2014)

Study size, design and location	Retrospective review of 163 patient records over 5.5 years (490 intracranial lesions) in the US. The 134 patients (82%) with follow-up imaging data available had 378 lesions and 39 post-operative cavities.
Intervention and comparator(s)	SIG-RS using Align RT alone to treat brain metastases (n=90) compared with surgery before SIG-RS (43); SIG-RS before WBRT (30); WBRT before SIG-RS (4). These data were compared with historical studies.
Key outcomes	The actuarial 12-month local control of the malignancy was 79% (71% to 86%) and the actuarial 12-month survival was 56% (95% CI 49% to 63%). This compares with previous frame-based and frameless studies reporting 12-month local control rates of 71% to 89% and 76% to 80% respectively, and survival rates of 33% to 37% and 40% to 44% respectively.
Strengths and limitations	Retrospective audit of patient notes with no comparator group; high overall mortality (73% dead at analysis; longest follow-up 45.1 months); this is in line with other similar studies in this area. This cohort overlaps with that reported by Pan et al. 2012.
Pan et al. (2012)	
Study size, design and location	Observational prospective study of 44 consecutive patients (115 intracranial metastases) in the US.
Intervention and comparator	SIG-RS to treat brain metastases (using AlignRT) compared with conventional frame-based or frameless stereotactic radiosurgery.
Key outcomes	The patients who received SIG-RS (AlignRT) alone (n=22) had similar clinical outcomes to those having conventional frame-based or frameless stereotactic radiosurgery.

Strengths and limitations	Small study with high overall mortality, which is typical for this patient group (70% dead at analysis; longest follow-up 21.6 months; median 6 months). The patients in this study were also included in the cohort reported by Pham et al. (2014).
Cervino et al. (2012)	
Study size, design and location	Observational study of 23 patients positioned using AlignRT without frames or masks. Positioning was confirmed using CBCT.
Intervention and comparator(s)	AlignRT and CBCT.
Key outcomes	Patient movement between the 2 methods of set-up and the time taken to complete the AlignRT procedure. The average movement after initial set-up with surface imaging was 1.85 mm in the anterior-posterior direction and <1.0 mm in the lateral and superior-inferior directions. Surface imaging with AlignRT took an average of 14 minutes out of the average total set-up time of 26 minutes including CBCT.
Strengths and limitations	A small study examining the feasibility of using AlignRT to position patients. Final positioning was confirmed by CBCT and not the AlignRT device; the latter was used during treatment.
Li et al. (2011)	
Study size, design and location	Comparative observational study including 15 patients and using a phantom head model to assess patient positioning accuracy.
Intervention and comparator(s)	AlignRT versus conventional frame-based SRS using CBCT.

Key outcomes	The accuracy of AlignRT in 1D motion detection was 0.1±0.1 mm using the head phantom. Head movement for SRS patients using a frame was <1.0 mm (0.3±0.2) and <1.0° (0.2±0.2) for 98% of the duration of treatment (1 patient had head rotation <1.5°). Similar movement was observed for AlignRT (0.3±0.2 mm and 0.2°±0.1°) and for 98% of the treatment time, the motion magnitude was <1.1 mm and <1.0°.
Strengths and limitations	This study was based on a small number of patients – only 4 patients in the frameless- (AlignRT) SRS group compared with 11 in the control framed-SRS group. Data gathered from phantom models may not reflect use in human studies.
Lau et al. (2015)	
Study size, design and location	Retrospective observational study on 15 patients in the US.
Intervention and comparator(s)	All positions were monitored using AlignRT during treatment.
Key outcomes	The 15 patients were treated for 62 metastases and followed up for an average of 7.1 months (1.1 to 24.3) or until death (11 patients). Treatment-related toxicity was below grade 3.
Strengths and limitations	This study was based on a small number of patients (15) and had no comparator group. It shows that the use of AlignRT in routine radiosurgery may provide similar outcomes to conventional radiosurgery.
Abbreviations: CBCT, cone beam CT; CI, confidence interval; SIG-RS, surface imaging-guided radiosurgery; SRS, stereotactic radiosurgery; WBRT, whole-brain radiation therapy.	

Recent and ongoing studies

No ongoing or in-development trials were identified.

Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

Two of 4 specialist commentators have used this technology before and 1 was familiar with it.

Level of innovation

The commentators agreed AlignRT was novel but not unique, and 1 thought it was highly innovative. One felt that this was the best system currently available. Two mentioned that the innovative aspect of AlignRT was avoiding the repeat X-ray images and radiation exposure as well as a greatly increased accuracy of patient positioning. One commentator felt that AlignRT may not be the best device for use with stereotactic radiosurgery (SRS) for secondary brain tumours, and that it might be better used for general radiotherapy. They noted that the NHS service specification for SRS uses other X-ray imaging.

Potential patient impact

Two commentators who had not used the device said that it would have little advantage over current methods of patient positioning for accurate radiosurgery. The 2 commentators who have used AlignRT thought it offered significant patient benefits in avoiding radiation exposure from additional X-rays and by halting the radiation beam when a person moves. It also allowed for a rapid readjustment of the person, minimising extra X-ray exposures and reducing anxiety. However, 1 expert noted that the radiation dose from imaging would be several orders of magnitude lower than the total radiation dose from treatment and so this would not be a particularly significant benefit from using AlignRT.

One expert (who had used the system in breast cancer treatment) noted a range of technical benefits including respiratory gating, tracking thoracic and abdominal respiratory

motion and compatibility with an automated treatment couch. One expert noted it was useful for people who couldn't tolerate a full-face mask and possibly for older patients. Another noted that children may benefit as well, but that the number of children being treated for these cancers would be very small.

One expert noted that dose and fractionation is standardised in the UK and so AlignRT would not alter the number of patient visits (fractions) or the amount of treatment radiation given. However, radiation from alternative imaging sources would be reduced.

Potential system impact

Two commentators said that AlignRT could lead to cost savings by increasing patient throughput because of quicker patient set-ups, and by using fewer time-consuming, radiation-based positioning methods. One also noted that using AlignRT would support a 'lean staffing' model, because it has the potential to allow staff of differing skill sets to set-up complex treatments safely and efficiently. Two commentators thought any advantages would be unclear or unlikely, with 1 noting that although AlignRT interrupts treatment if the patient moves, it does not correct for it, which may prolong treatment times.

When considering the potential cost impact of AlignRT, 1 commentator noted that standard linear accelerators (LINACs) have image-guidance systems already, such as cone beam CT, and so AlignRT would present an additional equipment cost. However, 1 commentator felt that AlignRT would allow SRS treatment on machines that do not have other specialist imaging. Another commentator queried how many head rests would be included in the purchase price and whether these may add costs.

Specialist commentators

The following specialists contributed to this briefing:

- Dr Keith Langmack, head of radiotherapy physics, Nottingham University Hospitals NHS Trust. No conflicts declared.
- Dr Owen Tilsley, consultant clinical oncologist, Velindre Cancer Centre. No conflicts declared.

- Ms Jacqui Dorney, UK specialist services lead at GenesisCare. Works for a commercial provider of radiotherapy services for breast cancer.
- Dr Richard Shaffer, consultant clinical oncologist, Royal Surrey County Hospital. Does private patient work with Genesis Care UK, who are currently considering purchasing AlignRT for several of their centres for non-stereotactic work. Also does work, currently unpaid, developing an intracranial stereotactic radiotherapy service, which may use AlignRT for patient positioning, for Genesis Care UK.

Development of this briefing

This briefing was developed by NICE. 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.

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