2009:23

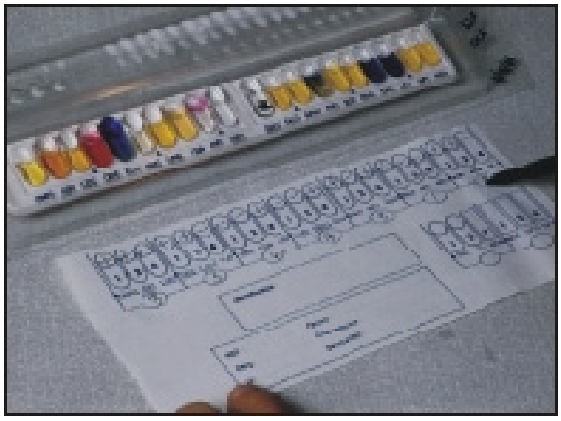
Health Technology Assessment

HTA-rapport

Intraoperativ magnetkameraundersökning på Neurooperation

VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

HTA-centrum



Vad är HTA?
HTA står för Health Technology Assessment – en systematisk granskning av den vetenskapliga dokumentationen för en metod eller teknologi inom hälso- och sjukvården. Avsikten med ett HTA-projekt är att värdera en viss teknik eller metod avseende.

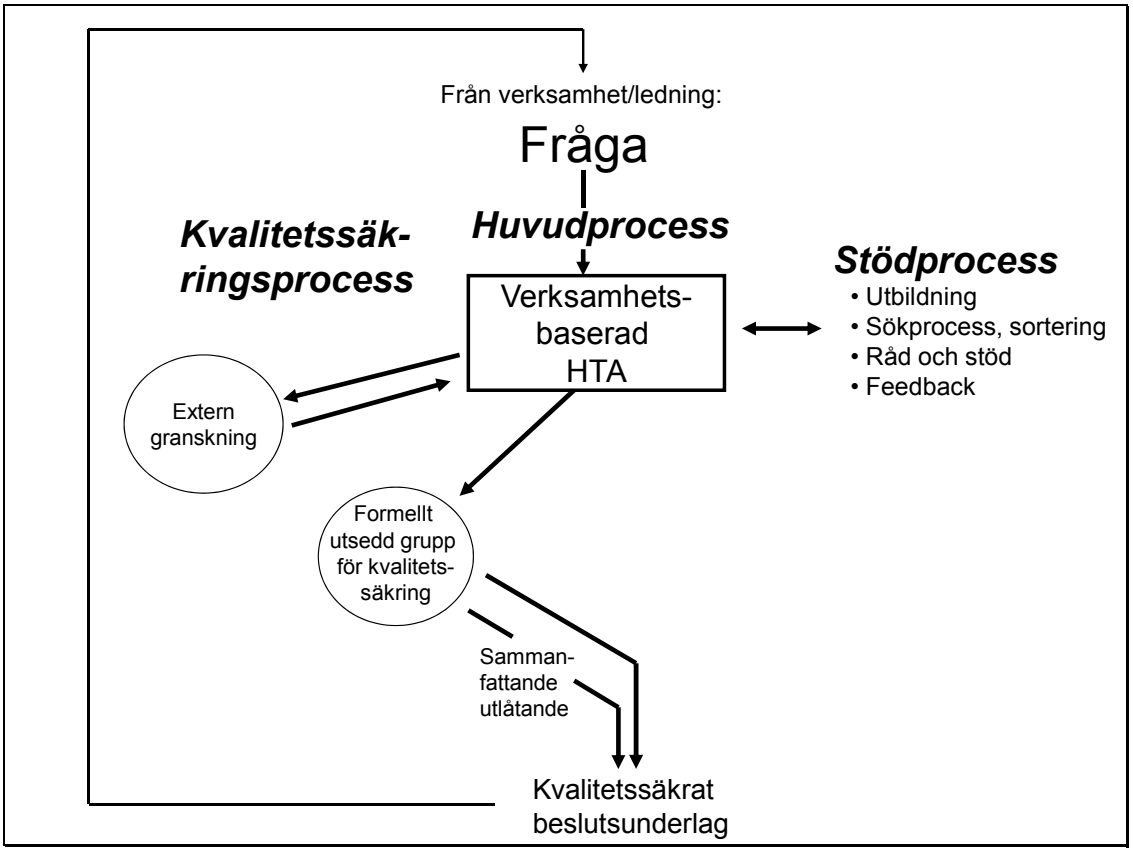
- Effekten i form av patientnytta och risker
- Etiska aspekter
- Organisatoriska aspekter
- Kostnader

HTA-centrum använder sig av det internationellt utarbetade GRADE-systemet för att gradera evidensstyrkan i det sammanlagda vetenskapliga underlaget för slutsatsen avseende en viss fråga. Evidensstyrkan graderas i fyra olika nivåer:

- Starkt vetenskapligt underlag = ⊕⊕⊕⊕ (Motsvarar tidigare Evidensgrad 1)
- Måttligt starkt vetenskapligt underlag = ⊕⊕⊕O (Motsvarar tidigare Evidensgrad 2)
- Begränsat vetenskapligt underlag = ⊕⊕OO (Motsvarar tidigare Evidensgrad 3)
- Otillräckligt vetenskapligt underlag = ⊕OOO (Motsvarar tidigare Evidensgrad 4)

I GRADE-systemet finns också en rekommendationsdel som inte används av HTA-centrum. Utvärderingen ger ändå vägledning för hälso- och sjukvården. Vid hög och måttlig evidensstyrka för slutsatsen att det finns en positiv effekt är underlaget gott och motiverar sannolikt att metoden tillämpas i hälso- och sjukvårdens kliniska vardag. Begränsad evidensstyrka för samma slutsats visar på att det finns ett visst vetenskapligt underlag som kan motivera att metoden används under förutsättning att andra krav på en acceptabel balans mellan nytta och risk, kostnadseffektivitet och etiska aspekter är uppfyllda. Om evidensstyrkan är otillräcklig indikerar det behov av mer forskning innan metoden börjar tillämpas i klinisk vardag.

Christina Bergh, professor, HTA-chef
HTA-centrum



Figuren visar schematisk HTA-centrums organisation uppdelat på huvudprocess, stödprocess och kvalitetssäkringsprocess.

Statement from the Regional HTA Centre of the Western Region in Sweden

Intraoperative Magnetic Resonance Imaging in Neurosurgery

The Regional Health Technology Assessment Centre (HTA-centrum) of the Western Region in Sweden (Region Västra Götaland, VGR) has the task to make statements on HTA reports carried out in VGR. The statement should summarise the question at issue, level of evidence, efficacy, risks, and economical and ethical aspects of the particular health technology that has been assessed in the report.

Associate professor Hans Silander, MD, PhD, and the Head of the Department of Neurosurgery, Sahlgrenska University (SU/S), Göteborg, Sweden, requested the present HTA.

A working group under the chairmanship of associate professor Bertil Rydenhag, senior consultant at the Department of Neurosurgery, SU/S, produced the HTA report. The other members of the working group were Hans Silander, senior consultant and head of the Department of Neurosurgery, Mats Johansson Högfeldt, senior consultant, Department of Neurosurgery, SU/S, Lars Jönsson, senior consultant, Department of Neuroradiology, SU/S, Thomas Skoglund, senior consultant, Department of Neurosurgery, SU/S and Göran Starck, associate professor Göran Starck, Dept. of Medical Physics and Biomedical Engineering, SU/S.

The participants from the HTA centre were Lennart Jivegård, MD, PhD, Ola Samuelsson MD, PhD, Therese Svanberg, librarian and information specialist, and Eva Alopaues, head of the library.

Thomas Lindén, M.D, PhD, and Karin Manhem, MD, PhD, have critically appraised the report.

Question at issue:

Does intraoperative MRI lead to better outcome in patients with intracerebral or pituitary tumours, and does it increase the neurosurgical precision?

PICO 1

P = Patients with brain tumour (intracerebral or pituitary tumour) subjected to neurosurgery
I = Intraoperative MRI
C = No intraoperative MRI
O = 1) Survival 2) Frequency of reoperations 3) Quality of life 4) Symptom relief 5) Degree of resection
6) Risks/Complications

PICO 2A

P = Patients operated for intracerebral tumours
I = Intraoperative MRI
C = Postoperative MRI within 72 hours
O = Concordance between the methods as evaluated by residual tumour volume (sensitivity/specificity)

PICO 2B

P = Patients operated for pituitary tumours
I = Intraoperative MRI
C = Postoperative MRI within 6 months
O = Concordance between the methods as evaluated by residual tumour volume (sensitivity/specificity)

Summary of the health technology assessment:

Method and patient category:
Most patients with glioma or pituitary adenoma undergo neurosurgery with the aim to remove as much tumour tissue as possible. The complex structure of the brain and the difficulties to exactly identify and visualize the exact borders of a tumour and the location of very important brain areas prompts further development of imaging of high accuracy during neurosurgical procedures. Intraoperative MRI (ioMRI) represents a technique with the potential to facilitate for the surgeon to remove as much tumour tissue as possible.

Level of evidence:
The systematic literature search identified one Canadian HTA-report from 2004. Articles published after 2004 included one study of moderate scientific quality that compared the use of low-to-mid field strength (0.2 T - 1.0 T) ioMRI with high-field strength (≥ 1.5 T) postoperative MRI with regard to survival, and one study of low scientific quality that compared the two with regard to the extent of surgical tumour resection. The former study did not show any difference in survival, and the latter reported a significantly greater extent of tumour tissue removal. The level of evidence with regard to these outcomes according to the GRADE system is ⊕OOO, i.e. insufficient.

Four studies were identified that evaluated the diagnostic performance of low-to-mid field ioMRI with high field MRI performed postoperatively. The diagnostic performance to detect residual tumour mass in patients with intracerebral tumours was evaluated in two studies, and to detect residual tumour mass in patients operated for pituitary tumours was evaluated in two studies. The sensitivity for intraoperative tumour detection in the studies of moderate scientific qualities varied between 82 - 100 %, and the specificity between 91 - 100 %. The level of evidence with regard to diagnostic performance is limited.

No study that compared the efficacy of ioMRI with postoperative MRI with regard to frequency of reoperations, quality of life or relief of symptoms was identified.

Risks
The use of ioMR was not associated with any risks for the patients.

Ethical aspects:
Is it ethically acceptable to perform neurosurgical procedures without the use of the ioMRI technique when there is some, albeit limited, scientific documentation that the extent of tumour removal is inferior without ioMRI. Surgery without ioMRI would then result in unnecessary repeated neurosurgical procedures, and may possibly result in less favourable overall outcome for patients who require neurosurgery for intracerebral or pituitary tumours.

Economical aspects
Data are incomplete and sparse. Rough estimations indicate that the cost of each procedure will increase by 19%. However, the need for reoperations will most probably decrease but it is not possible to estimate how much this will reduce overall cost. Therefore, presently the total change of cost is difficult to define.

Concluding remarks

The scientific documentation of the eventual beneficial effects of intraoperative MR on survival is insufficient (⊕OOO).

The scientific documentation of the potential beneficial effects of intraoperative MR with regard to surgical precision, i.e. the extent of tumour tissue removal, is insufficient (⊕OOO).

The scientific documentation of intraoperative MR as a diagnostic tool during neurosurgery is limited.

On behalf of HTA-centrum Göteborg, Sweden, 2009-12-09

Christina Bergh, Professor, MD.
Head of HTA-centrum

Eva Alopaeus, Chief librarian	Lennart Jivegård, Associate professor	Maria Skogby PhD
Magnus Hakeberg, Professor	Anders Larsson Associate professor	Annika Strandell Associate professor
Hans Hedelin, Professor,	Ola Samuelson, Associate professor	Therese Svanberg Librarian
Peter Johansson PhD	Henrik Sjövall Professor	Åsa Axelsson Associate professor

Utlåtande och sammanfattande bedömning från Kvalitetssäkringsgruppen

Intraoperativ magnetkameraundersökning på Neurooperation

HTA-kvalitetssäkringsgruppen har ett uppdrag att yttra sig över genomförda HTA i Västra Götalandsregionen. Yttrandet skall innefatta sammanfattning av frågeställning, samlat evidensläge, patientnytta, risker samt ekonomiska och etiska aspekter för den studerande teknologin.

Denna HTA har genomförts på begäran av verksamhetschef Hans Silander, Neurosjukvården, Sahlgrenska Universitetssjukhuset (SU/S).
En arbetsgrupp bestående av Mats Johansson Högfeldt, överläkare, Neurooperation, SU/S, Lars Jönsson, överläkare, Neuroradiologi, SU/S, Bertil Rydenhag, överläkare, avd. för Neurokirurgi, SU/S, Thomas Skoglund, överläkare, avd. för Neurokirurgi, SU/S och Göran Starck, docent, 1:e ingenjör Radiologisk fysik, SU/S har tillsammans med HTA-centrum tagit fram HTA-rapporten.

Resurspersoner från HTA-centrum har varit Ola Samuelsson, docent, Lennart Jivegård, universitetslektor, Therese Svanberg, bibliotekarie, och Eva Alopaues, bibliotekschef.

HTA-rapporten samt åberopad och förtecknad litteratur har granskats av Karin Manhem, docent, Medicin, SU/Mölndal, och Tomas Lindén, docent, Rehabiliteringsmedicin, SU/S.

Slutsatser har diskuterats vid möten mellan HTA-centrum och HTA-projektgruppen. Ett utlåtande har tagits fram, diskuterats och fastställts vid HTA-kvalitetssäkringsgruppens möte 2009-12-09.

Projektet har pågått under perioden 2009-05-06—2009-12-09.
Den systematiska litterurgenomgången omfattade perioden november 2003 t.o.m. augusti 2009.

Frågeställning:
Leder användning av intraoperativ magnetkamera (MR) till ökad kirurgisk precision och därmed till en bättre överlevnad och ett mer fullständigt borttagande av intracerebrala tumörer och hypofystumörer?

PICO 1:
P = Patienter som opereras för hjärntumör (intracerebral tumör eller hypofystumör)
I = Intraoperativ MR
C = Ingen intraoperativ MR
O = Primärt utfall:
Överlevnad
Sekundära utfall:
1. Frekvens reoperationer 2. Livskvalitet 3. Symtomförbättring 4. Resektionsgrad
5. Komplikationer

PICO 2A och 2B:
P = Patienter som opereras för intracerebral tumör (2A) eller hypofystumör (2B)
I = Intraoperativ MR
C = Postoperativ MR inom 72 timmar (2A) eller 6 månader (2B)
O = Diagnostik säkerhet avseende kvarstående (”residual”) tumörvolym (sensitivitet/specificitet)

Resultatet av HTA-processen:

Metod och målgrupp:
Det primära målet med neurokirurgi hos patienter som opereras för en hjärntumör är att ta bort så mycket av tumören som möjligt. På grund av hjärnans komplexa och känsliga struktur och svårigheter att med ögat se exakt var tumören gränsar mot normal hjärnvävnad är det svårt att under operationen avgöra hur mycket tumörvävnad som har avlägsnats. Intraoperativ MR med ”låg-fältsteknik” är en teknik som kan vägleda och hjälpa kirurgen att ta bort så mycket tumörvävnad som möjligt utan att skada känsliga och friska delar av hjärnan.

Evidensläge för studerad patientnytta:
Den systematiska litteraturöversikten identifierade en kanadensisk HTA-rapport från 2004. Den konstaterade att användbarheten och effektiviteten av intraoperativ MR inte var klarlagd. Efter 2004 har det publicerats en ny studie som jämför överlevnaden och en andra studie som studerat hur stor del av den ursprungliga tumörvävnaden som avlägsnats hos patienter som opererats med hjälp av intraoperativ MR jämfört med patienter som opererats utan sådan intraoperativ vägledning. Den första studien har medelhög vetenskaplig kvalitet men visade ingen signifikant skillnad i överlevnad. Den andra studien fann att intraoperativ MR ledde till ett signifikant bättre operationsresultat. Den var emellertid av låg vetenskaplig kvalitet.
Det vetenskapliga underlaget för intraoperativ MR vid operation av patienter med hjärntumör är avseende såväl överlevnad som resektionsgraden av tumörmassan otillräckligt (Evidensgrad enligt Grade-systemet: ⊕OOO).

Två studier, en av medelhög och en av låg kvalitet, har utvärderat diagnostiska prestanda av intraoperativ ”låg-fälts” MR med postoperativ ”hög-fälts” MR hos patienter som opererats för intracerebral tumör. Två studier, en av medelhög och en av låg kvalitet, har gjort samma typ av jämförelse hos patienter som opererats för hypofystumör. I de två studierna med medelhög kvalitet var sensitiviteten 82 – 89 % och specificiteten 90 -100 %.
Det vetenskapliga underlaget för intraoperativ MR som diagnostiskt hjälpmedel vid operation av patienter med hjärntumör är begränsat.

Det saknas jämförande studier av effekten av intraoperativ MRI avseende frekvensen av reoperationer, påverkan på livskvalitet och eventuell symtomförbättring.

Risker
Användning av intraoperativ MR har inte visat sig vara förenat med några risker för patienterna.

Etiska aspekter:
Är det försvarbart att fortsätta operera patienter med hjärntumör utan vägledning av intraoperativ MR när tekniken har potential att öka den diagnostiska säkerheten i bedömningen av hur mycket tumör som kan tas bort?

Ekonomiska aspekter
Den slutliga kostnadsförändringen till följd av investering och användning av en magnetkamera som kan användas intraoperativt är mycket svår att bedöma. Kostnaden per operation uppskattas att öka med cirka 20%, medan antalet reoperationer med största sannolikhet kommer reduceras. Om detta leder till en total kostnadsökning eller besparing kan för närvarande inte beräknas.

Sammanfattning och slutsats

Det vetenskapliga underlaget för intraoperativ MR med avseende på eventuell förbättrad överlevnad är otillräckligt (⊕OOO).

Det vetenskapliga underlaget för intraoperativ MR med avseende på eventuell förbättrad kirurgisk precision, dvs. volym av tumörmassan som avlägsnas vid en operation, är otillräckligt (⊕OOO).

Det vetenskapliga underlaget för intraoperativ MR som diagnostiskt hjälpmedel vid operation av patienter med hjärntumör är begränsat.

För HTA-kvalitetssäkringsgruppen 2009-12-09

Christina Bergh
Ordförande

HTA-kvalitetssäkringsgruppen:

Eva Alopaeus, Bibliotekschef	Lennart Jivegård, Universitetslektor	Maria Skogby Med. dr
Magnus Hakeberg, Professor	Anders Larsson Docent	Annika Strandell Docent
Hans Hedelin, Professor,	Ola Samuelson, Docent	Therese Svanberg HTA-bibliotekarie
Peter Johansson Med. Dr.	Henrik Sjövall Professor	Åsa Axelsson Docent

Litteraturlista: enligt redovisning i HTA:n

Table of content

Which health technology or method will be assessed?

INTRAOPERATIVE MAGNETIC RESONANCE IMAGING IN NEUROSURGERY

1a. **Who will lead the project?**

Bertil Rydenhag, MD, PhD, Dept. of Neurosurgery, Sahlgrenska University Hospital

b. **Who posed the question?**

Mats Johansson Högfeldt, MD, Dept. of Neurosurgery, Sahlgrenska University Hospital

c. **Additional parties who posed the question?**

Hans Silander, MD, PhD, Dept. of Neurosurgery, Sahlgrenska University Hospital

Co-workers in the work group**:**
Thomas Skoglund, M.D, PhD, Dept. of Neurosurgery, Sahlgrenska University Hospital
Lars Jönsson, M.D,.PhD, Dept. of Neuroradiology, Sahlgrenska University Hospital
Göran Starck, PhD, Dept. of Medical Physics and Biomedical Engineering, Sahlgrenska University Hospital
Mats Johansson Högfeldt, M.D, Dept. Of Neurosurgery Sahlgrenska University Hospital

d. **Other participants, from the HTA centre and external reviewers**

Ola Samuelsson, M.D, PhD, Dept. of Nephrology, Sahlgrenska University Hospital
Lennart Jivegård, M.D, PhD, Dept. of Vascular Surgery, Sahlgrenska University Hospital
Therese Svanberg, librarian, Sahlgrenska University Hospital
Eva Alopaeus, chief librarian, Sahlgrenska University Hospital

External reviewers:
Thomas Lindén, M.D, PhD, Dept of Medical Rehabilitation, Sahlgrenska University Hospital
Karin Manhem, M.D, PhD, Dept of Internal Medicine, Sahlgrenska University Hospital

e. **Are there any conflicts of interest for the proposer or any of the participants in the work group?**
No.

Disease/disorder of Interest and Present Treatment

2a. **Disease/disorder of interest and its degree of severity**

Patients with glioma or pituitary adenoma undergoing intracranial neurosurgical procedure.

- ✓ Risk of premature death
- ✓ Risk of permanent illness or damage, or reduced quality of life
- ✓ Risk of disability and health-related quality of life

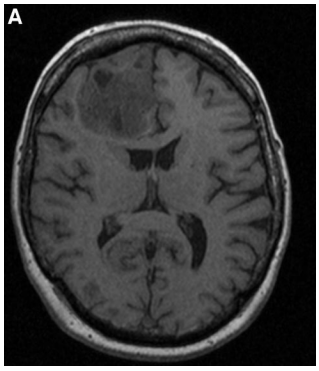
b. **Prevalence and incidence of the disease/disorder**

The number of neurosurgical procedures performed on patients with tumours of different types can be estimated to about 150/year at the Department of Neurosurgery, Sahlgrenska University Hospital, Göteborg. This estimation is made from the annual production data in the standard database at the hospital for several years.

c. **Present treatment of the disease/disorder in the outpatient setting/ in-patient setting**

Patients with gliomas or pituitary adenomas are normally referred to the neurosurgical department. After preoperative work-up a decision is made whether the tumour is suitable for surgical removal.

The prognostic outlook for the patient, i.e. the life expectancy, is considered to be correlated with the extent of surgical resection of the tumour. There is a general agreement that if the tumour is radically resected the survival is better. A recent meta-analysis (Sanai et al. 2008) found that in patients with a low-grade glioma there was a difference in five-year survival from 40 % following a biopsy with no surgical tumour resection up to 90 % following gross total tumour removal. A possible bias of this analysis may be that the decision to only perform a biopsy without further surgical intervention may be a judgment of inoperability. For patients with a high-grade glioma another meta-analysis has reported that there was a difference in the mean survival time of 8 months for small incomplete resections up to 22 months for 100 % resection without any postoperative residual tumour (Lacroix et al. 2001). One of the studies in this latter meta-analysis reported that the extent of the resection should be more than 98 % for a significant prolongation of survival, similar results are presented by another group (Stummer et al. 2008). There is also some support that quality of life is increased following radical tumour resection (Brown et al. 2005).



In neurosurgery, preoperative MR imaging and intraoperative neuronavigation, based on preoperative investigations has been developed and applied routinely for more than a decade. The preoperative work-up includes a magnetic resonance imaging (MRI) examination using diagnostic high field strength MRI equipment. This examination provides detailed images of the tumour and enables the surgeon to

decide whether complete resection of the tumour is possible or not. However, this preoperative information is only of limited use intraoperatively since anatomic alterations are caused by surgical retraction, cerebrospinal fluid changes and tumor removal during the surgical procedure. Therefore, presently many patients are sent to postoperative MRI examination immediately after the neurosurgical procedure. The patient is transported, during general anesthesia, to the MRI unit, which in the Sahlgrenska University Hospital is quite remote from the operating room.
If there is remaining tumour suitable for further resection the patient is transported back to the operating room and the surgery is pursued. Thus, the imaging sessions are presently not an integral part of the surgical procedure.

Some patients are presently examined postoperatively by MRI or CT the day after surgery, or even later, when awake.

Patients who undergo neurosurgery for intracranial tumours normally remain at the neurosurgical ward for about five days.

The complex structure of the brain and the difficulties to exactly identify and visualize the exact borders of a tumour and the location of very important brain areas prompts further development of imaging of high accuracy during neurosurgical procedures.

d. **Number of patients per year who undergo current treatment regimen?**

About 150 patients per year.

e. **The normal pathway of a patient through the health care system**

As described above (see 2c) a patient with an intracerebral tumour is normally referred to the Department of Neurosurgery. After preoperative work-up a decision is made whether the tumour is suitable for surgical removal, and following surgery a postoperative MRI or CT is done to validate the extent of the surgical procedure. This is done during the stay at the neurosurgical ward or during the next couple of weeks when the patient has been discharged from the hospital. Further follow-up is done on an outpatient basis. For some groups of patients the first postoperative imaging investigation is made even later, 3-6 months (pituitary tumours).

f. **Actual wait time in days for medical assessment /treatment**

Patients are typically scheduled for surgery within 2-3 weeks after first referral to the Department of Neurosurgery.

Present Health Technology

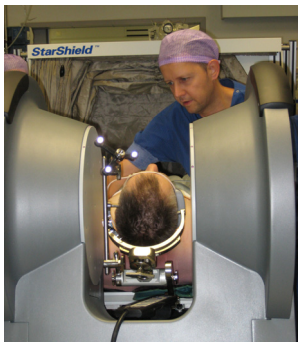
3a. **Name/description of the health technology at issue**

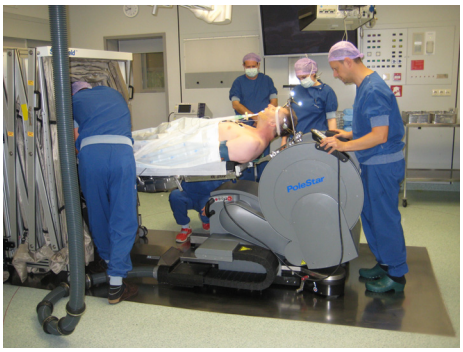
Intraoperative MRI in neurosurgical procedures for gliomas and pituitary adenomas.

b. **The work group's understanding of the potential value of the health technology**

The currently used peroperative investigations and neuronavigation procedures lack high precision and accuracy due to the successive movements and the brain shift that occur during certain surgical procedures. Furthermore, in some procedures, the surgeon´s field of view is restricted leading to difficulties in performing optimal removal of a tumour. Therefore, there is a need to improve the visualisation of tumour tissue and important structures inside the brain to enable optimal tumour resection without jeopardising neurological functions.

Intraoperative MRI represents a technique with the potential to facilitate for the surgeon to remove as much tumour tissue as possible. The immediate benefit for the patient of such a technique is more extensive tumour removal, and, consequently, probably a better outcome with a longer life expectancy, a need of fewer reoperations and less secondary neurological deficits.





Intraoperative MRI (ioMRI) has been utilized in neurosurgery in some centres for more than a decade, but is not in routine clinical use. The development of the ioMRI equipment occurs along two different lines. One is the development of equipment with low field strength and reasonable small physical dimensions, suitable for the integration with other equipment in an ordinary operating room. The low field strength MRI has the advantage of relatively low total cost and an easy integration in the conventional neurosurgical workflow. Disadvantages, however, are low magnetic field strength and, a a result of the small physical dimensions, rather poor magnetic field homogeneity, leading to lower image quality compared with diagnostic low-to-mid-field (0.2 T – 1.0 T) or high-field (≥ 1.5 T) MRI. Still, the image quality may be sufficient to enable the detection of tumour remnants and to update the neuronavigation images. The other line of development is the adaptation of diagnostic mid-field or high-field strength MRI equipment for intraoperative imaging with diagnostic potential. This type of equipment can also be used for

whole body investigations. The level of investment, the demands on the building and on the other equipment in the operating room are much higher for this concept.

Future use of ioMRI also for other neurosurgical indications is forthcoming. It has been used in epilepsy surgery patients with intractable seizure situations. Imaging during the surgical procedure with low-field ioMRI has increased the accuracy of the extent of resection/ transsection of the brain tissue.

In "Västra Götalandsregionen" (western region of Sweden) a low-field ioMRI facility should preferably be installed in the neurosurgical operating theatre at the Sahlgrenska University Hospital. Thereby, it will become an integral part of the neurosurgical procedure.

The number of patients may be estimated to about 150 per year (see 2d). There will be no essential difference in workflow or impact on the processing of the patients through the hospital. Furthermore there will be no major shift in the utilisation of the present diagnostic MRI equipments although a more limited use of both preoperative investigations for neuronavigational purposes and direct postoperative investigations can be foreseen. The ioMRI investigation will primarily just add a couple of imaging scans during the actual surgical procedure. There will be no replacement for other procedures or intraoperative techniques.

c. **The question(s) at issue for the current HTA project in one sentence**

Does intraoperative MRI lead to better outcome in patients with intracerebral or pituitary tumours, and does it increase the neurosurgical precision?

d. **PICO**

PICO 1
P = Patients with brain tumour (intracerebral or pituitary tumour) subjected to neurosurgery
I = Intraoperative MRI
C = No intraoperative MRI
O = 1) Survival
2) Frequency of reoperations
3) Quality of life
4) Symptom relief
5) Degree of resection
6) Risks/Complications

PICO 2A
P = Patients operated for intracerebral tumours
I = Intraoperative MRI
C = Postoperative MRI within 72 hours
O = Concordance between the methods as evaluated by residual tumour volume (sensitivity/specificity)

PICO 2B
P = Patients operated for pituitary tumours
I = Intraoperative MRI
C = Postoperative MRI within 6 months
O = Concordance between the methods as evaluated by residual tumour volume (sensitivity/specificity)

e. **Key words**

Neuroimaging, intraoperative MRI, brain tumour

Review of the Level of Evidence

4. **Search strategy, study selection and references – appendix 3**

During May, 2009, with an update in August, the library performed searches in PubMed, the Cochrane Library, CINAHL, AMED and a number of HTA-databases. (See appendix 3 for details). Reference lists of relevant articles were also scanned for additional references. A total of 826 articles were identified, of which 778 abstracts were excluded by the library and by one member of the work group (HS). Another 38 articles were excluded after having been read in full text. Ten articles were sent to the whole work group. Seven of these articles are included in the report and have been critically appraised. The appraisal of the articles is based on checklists from SBU (2008), which were developed by Professor Olle Nyrén, Karolinska Institutet, Stockholm.

Search strategies, eligibility criteria and a graphic presentation of the selection process together with reference lists are presented in appendix 3.

All searches were made by two librarians (EA and TS).

5a. **Describe briefly the present knowledge of the health technology**

A recent HTA-report from Canada stated in 2004 that there is a shortage of published articles of good scientific quality relevant for the use of the intraoperative MRI technique (Scott 2004). It concluded that the scope, applicability, efficacy, and cost effectiveness had not been established yet.

The systematic literature search of articles published after November 2003 identified seven relevant studies .One study compared the use of ioMRI with postoperative MRI with regard to survival, and one study compared the two with regard to the extent of surgical tumour resection. The former study was of moderate scientific quality but did not show any difference in survival. The other study reported a significantly greater extent of tumour tissue removal. However, this study was of low scientific quality.

According to the GRADE system the level of evidence with regard to survival and extent of tumour tissue removal is ⊕OOO, i.e. insufficient.

Five studies evaluated the diagnostic performance of intraoperative with postoperative MRI. In four of these five studies low-field ioMRI was compared with postoperative high-field MRI.

The diagnostic performance of low-field ioMRI to detect residual tumour mass in patients with intracerebral tumours was evaluated in two studies. One study was of moderate and the other of low scientific quality. The sensitivity and specificity for intraoperative tumour detection in the former study were 82 % (95 % CI: 0.59 –

0.94%), and 95 % (95 % CI: 0.73 – 1.0), respectively. The presentation of data in the latter did not allow calculation of sensitivity and specificity.

The diagnostic performance of ioMRI in patients operated for pituitary tumours was evaluated in three studies. One study was of moderate and two were of low scientific quality. The study of moderate scientific quality reported a sensitivity to detect residual tumour mass with low-field ioMRI of 88.9 % (95 % CI: 0.517 – 0.997), 85.7 % (95 % CI: 0.572 – 0.982), 93.3 % (95 % CI: 0.81 – 0.998), and 100 % (95 % CI: 0.664 – 1.00) for the suprasellar, intrasellar, right, and left parasellar regions, respectively. Specificity to detect residual tumour mass for the same regions, defined as correct identification of complete resection, was of 90.5 % (95 % CI: 0.696 – 0.983), 100 % (95 % CI: 0.794 – 1.00), 100 % (95 % CI: 0.782 – 1.00), and 100 % (95 % CI: 0.839 – 1.00). The presentation of data in one study of low scientific quality did not allow calculation of sensitivity and specificity. Furthermore, in this study high-field MRI was used for the intraoperative imaging. In the other study of low scientific quality the sensitivity and specificity could be calculated to be 62.5 % (95 % CI: 0.26 – 0.89), and 97.6 % (95 % CI: 0.86 – 0.99).

The sensitivity and specificity data can also be expressed in other words. The sensitivity data from the studies of moderate scientific quality mean that when low-field ioMRI is used during neurosurgical procedures of brain tumours, 82 -100% of all the patients who have remaining tumour tissue after the initial surgical removal can correctly be detected already during the same surgical session in the operating room. This will then allow immediate further resection instead of a reoperation some days later. The specificity data mean that 90 -100% of the cases with complete tumour removal will be correctly identified with the ioMRI. This means that in only 0-10% of the patients there is a risk for unnecessary further reoperations.

The level of evidence with regard to diagnostic performance is limited.

There was no study that compared the use of ioMRI with postoperative MRI with regard to frequency of reoperations, quality of life and relief of symptoms.

b. **Outcome tables of included studies**

Appendix 1a. Survival
Appendix 1b. Degree of resection
Appendix 1c. Diagnostic performance

c. **Excluded articles – appendix 2**

d. **Ongoing research**

To our knowledge, there are several centres in Europe and North America conducting feasibility studies in neurosurgical applications of intraoperative MRI.

Intraoperative MRI equipment has not yet been installed in any Swedish hospital.

6 **Which medical societies or health authorities recommend the new health technology?**

There are no national or international recommendations.

Ethical aspects

7a. **Ethical consequences**

There are no major negative consequences in using the ioMRI technique. In contrast, an ethical dilemma is that neurosurgical procedures performed without the use of the intraoperative MRI technique, may prove to be inferior. This would then result in unnecessary repeated neurosurgical procedures, and less favourable overall outcome for patients requiring neurosurgery for intracerebral or pituitary tumours.

b. **Will other patient groups or other treatments be adversely affected (pushed aside) due to an introduction of the new health technology?**

The ioMRI technology will lengthen the surgical operating time. Thus, fewer procedures in the same operating room will be carried out within the same timeframe available for surgery. However, the neurosurgical precision will increase, and, thereby, result in a decreased need of reoperations for intracerebral tumours. Considering the potential of a decrease in the number of reoperations and a moderate increase in time for the surgical procedures the net increase of operating time will be limited.

Organisation

8a. **When can the new health technology be put into practice?**

An operating room could be ready for use within a maximum of three months after the delivery of ioMRI equipment. During this period necessary modifications of the operating room will be completed, and the education of involved categories of medical staff will be carried out.

b. **Is this technology used in other hospitals in the Western Region of Sweden?**

No, the equipment at issue is specifically designed for neurosurgery. This is only available at the Sahlgrenska University hospital.

c. **According to the work group, will there be any consequences of the new health technology for personnel?**

The installation of intraoperative MRI equipment should follow the general scheme for introduction of new equipment at the hospital. Most probably it will not have any negative effects of the physical environment in the operating room. The additional hazards of the electromagnetic fields of the ioMRI system must be handled in the physical environment. Similar precautions need to be carried out as for the installation and the use for other diagnostic MRI equipment. Information as

well as education of radiologists, technicians, neurosurgeons and different categories of the medical staff at the neurosurgical operating room must be given.

d. **Will there be any consequences for other clinics or supporting functions at the hospital or in the whole Western Region of Sweden?**

The main impact will be seen at the Department of Radiology. Both technical and diagnostic support to the neurosurgeons may be required. However, it is the ambition that the technique may also be mastered by the neurosurgeons themselves.

Economy

9a. **Present costs of currently used technologies**

The average total hospital cost per patient based on data from 2008 was 124 000 SEK. The annual cost for a total of 150 patients with the use of the presently used surgical routine would therefore be 18.6 million SEK.

b. **Expected costs of the new health technology**

The total investment cost can be estimated to 15 million SEK, and the total pay off time is set to 7 years (1050 investigations in total and 150 investigations per year). The cost for a full service contract is about 800 000 SEK/year, and the cost directly related to each procedure is estimated to be about 3 000 SEK. Based on these figures a rough estimate of the total cost (including an interest rate for the investment set to 4%) per investigation is 25 000 SEK.

c. **Total change of cost**

It is difficult to estimate the total net-cost or net-saving of intraoperative MRI, since both the need for preoperative MRI investigations for neuronavigation definitely will decrease as well as the number of necessary postoperative radiological examinations. Furthermore, the need for reoperations is also expected to decrease. Taken together, there is a definite potential for a net reduction of the present costs for the care of neurosurgical patients. However, presently there are no valid data for a detailed calculation of the total change of cost.

d. **Can the new technology be adopted and used within the clinic budget/ hospital budget?**

It is probably not possible to finance this technology with the present economical resources at the hospital level or at the department level. Consequently, financing should be made at the regional level.

e. **Are there any available analyses of health economy? Cost advantages or disadvantages?**

There are no valid data on the cost-effectiveness of this new technology.

Unanswered Questions

10a. **Important gaps in scientific knowledge?**

It is still not established whether a greater extent of tumour resection following the use of intraoperative low-field MRI examinations will result in a better overall survival and lesser neurological functional deficits. This would need a randomized trial of sufficient sample size and time of follow-up, in which patients are randomised to either the conventional surgical routine or to surgery using intraoperative MRI.

However, due to the rather long survival-time of patients with low-grade gliomas (which is an important group in this context), and that patients have individual tumours affecting different parts of the brain with different surgical accessibility, and to the fact that not all patients will tolerate postoperative cytotoxic and/or radiotherapeutical treatment it will be very difficult to perform a proper prospective long-term, randomised study.

b. **Is there any interest in your own clinic/research group/organisation to start studies/ trials within the research field at issue?**

A collaborative study between Swedish neurosurgical centres to study the efficacy of intraoperative MRI to radically decrease the amount of residual tumour tissue in procedures performed by different neurosurgeons at different hospitals would be of great interest. If the success rate of complete tumour removal observed at the immediate postoperative MRI can be shown to increase up to 95-100 % then the new MRI technique must be considered to be very useful.

Summary of the Health Technology Assessment

- **Method and patient group**
  Most patients with glioma or pituitary adenoma undergo neurosurgery with the aim to remove as much tumour tissue as possible. The complex structure of the brain and the difficulties to exactly identify and visualize the exact borders of a tumour and the location of very important brain areas prompts further development of imaging of high accuracy during neurosurgical procedures. Intraoperative MRI (ioMRI) represents a technique with the potential to facilitate for the surgeon to remove as much tumour tissue as possible.

- **Questions at issue**
  Does intraoperative MRI lead to better outcome in patients with intracerebral or pituitary tumours, and does it increase the neurosurgical precision?

- **PICO 1**
  P = Patients with brain tumour (intracerebral or pituitary tumour) subjected to neurosurgery
  I = Intraoperative MRI
  C = No intraoperative MRI
  O = 1) Survival 2) Frequency of reoperations 3) Quality of life 4) Symptom relief 5) Degree of resection 6) Risks/Complications

  PICO 2A and 2B
  P = Patients operated for intracerebral tumours (2A) or for pituitary tumours (2B)
  I = Intraoperative MRI
  C = Postoperative MRI within 72 hours (2A) or within 6 months (2B)
  O = Concordance between the methods as evaluated by residual tumour volume (sensitivity/specificity)

- **Studied risks and benefits for patients of the new health technology**
  The systematic literature search identified one Canadian HTA-report from 2004. Articles published after 2004 included one study of moderate scientific quality that compared the use of ioMRI with postoperative MRI with regard to survival, and one study of low scientific quality that compared the two with regard to the extent of surgical tumour resection. The former study did not show any difference in survival, and the latter reported a significantly greater extent of tumour tissue removal. The level of evidence with regard to these outcomes according to the GRADE system is ⊕OOO, i.e. insufficient.

  Five studies were identified that evaluated the diagnostic performance of low field ioMRI with high field MRI performed postoperatively. The diagnostic performance to detect residual tumour mass in patients with intracerebral tumours was evaluated in two studies, and to detect residual tumour mass in patients operated for pituitary tumours was evaluated in three studies. The sensitivity for intraoperative tumour detection in two studies of moderate scientific qualities varied between 82 - 100 %, and the specificity between 91 - 100 %. The level of evidence with regard to diagnostic performance is limited.

- **Ethical questions**
  Is it ethically acceptable to perform neurosurgical procedures without the use of the ioMRI technique when there is some, albeit limited, scientific documentation that the extent of tumour removal is inferior without ioMRI. Surgery without IOMRI would then result in unnecessary repeated neurosurgical procedures, and less favourable overall outcome for patients requiring neurosurgery for intracerebral or pituitary tumours.

- **Economical aspects**
  Data are incomplete and sparse. Rough estimations indicate that the cost of each procedure will increase by 20 %. However, the need for reoperations will decrease but it is not possible to estimate how much this will reduce the overall cost. Therefore, presently, the total change of cost is difficult to define.

Appendix 1 a

Included articles

Outcome variable: Survival

Author, year, country, reference no	Study design, number of patients, withdrawals/drop-outs	Result Intervention and control group	Complications/ Comments	Quality of study
Hirschberg 2005, Norway	Non-randomised, controlled study 64 patients with high-grade gliomas: -32 patients operated on using mid-field ioMRI -32 patients operated on without ioMRI (conventional group) No withdrawals or drop-outs	Survival: - ioMRI group: 14.5 months (95 % CI: 12.0 – 16.6) - conv. group: 12.1 months (95 % CI: 10.2 – 14.1)	No differences in post-operative neurological deficits No differences in post-operative infections Longer operating time: 5 hrs vs 3.4 hrs.	Moderate

Abbreviation. ioMRI = intraoperative magnetic resonance imaging

Appendix 1 b

Included articles

Outcome variable: Degree of resection

Author, year, country, reference no	Study design, number of patients, withdrawals/drop-outs	Result Intervention and control group	Complications/ Comments	Quality of study
Bergsneider, 2005, USA	Retrospective study 48 patients with supratentorial gliomas: -13 patients operated on using mid-field (0.2 T) diagnostic MR system for ioMRI -12 patients operated on without ioMRI (conventional group) -10 +13 patients operated on using high-field ioMRI No withdrawals or drop-outs	Percent resection of tumour volume: - ioMRI group: 91 (s.d. 7) - conv. group: 79 (s.d 24) Postoperative tumour volume (cm^3): - ioMRI group: 4.2 (s.d. 3.8) - conv. group: 13.0 (s.d 14)	No differences in permanent post-operative neurological deficits	Low

Abbreviation. ioMRI = intraoperative magnetic resonance imaging

Appendix 1 c

Included articles

Outcome variable: Diagnostic performance (Sensitivity and specificity)

Author, year, country, reference no	Study design, number of patients, withdrawals/drop-outs	Result Intervention and control group	Complications/ Comments	Quality of study
Hirschl, 2009, USA	Diagnostic study 42 patients with gliomas Low-field ioMRI compared with high-field postoperative MRI (as reference method) No withdrawals or drop-outs	Prevalence of residual tumour tissue: - Sensitivity: 82 % (95 % CI: 59 – 94) - Specificity: 95 % (95 % CI: 73 – 100)	The field strength of the ioMRI was 0.12 T.	Moderate
Senft, 2008, Germany	Diagnostic study 63 patients with gliomas Low-field ioMRI compared with high-field postoperative MRI (as reference method) No withdrawals or drop-outs	Prevalence of residual tumour tissue: True positive (TP) findings in 38 patients and true negative (TN) finding in 1 patient. No data given of false positive (FP) and false negative (FN) findings. Thus, sensitivity and specificity cannot be calculated.	The field strength of the ioMRI was 0.15 T.	Low

<table>
<tr>
<td>Nimsky, 2006, Germany</td>
<td>Diagnostic study

106 patients with pituitary adenomas

High-field (1.5 T) diagnostic MR system for ioMRI compared with high-field postoperative MRI (as reference method)

One patient died within 2 days postoperatively</td>
<td><u>Prevalence of residual tumour tissue:</u>
Data on TP, TN, FP, FN are incomplete and sensitivity and specificity cannot be calculated.

IoMRI increased the rate of complete tumour removal from 58 % (49 of 85 patients) to 82 % (70 of 85 patients)</td>
<td>The postoperative MRIs were performed after 7 days and 3 months.</td>
<td>Low</td>
</tr>
<tr>
<td>Gerlach, 2008, Germany</td>
<td>Diagnostic study

40 patients with pituitary adenomas

Low-field ioMRI compared with high-field postoperative MRI (as reference method)

No withdrawals or drop-outs</td>
<td><u>Prevalence of residual tumour tissue:</u>

Sensitivity (%, 95 CI in parentesis)
<table>
<tr><th>Supra-sellar</th><th>Intra-sellar</th><th>Right parasellar</th><th>Left parasellar</th></tr>
<tr><td>89
(52 – 100)</td><td>86
(57 – 98)</td><td>83
(8 – 99)</td><td>93
(66 – 100)</td></tr>
</table>
Specificity (%, 95 CI in parentesis)
<table>
<tr><th>Supra-sellar</th><th>Intra-sellar</th><th>Right parasellar</th><th>Left parasellar</th></tr>
<tr><td>91
(70 – 98)</td><td>100
(79 – 100)</td><td>100
(78 – 100)</td><td>100
(84 – 100)</td></tr>
</table></td>
<td>The field strength of the ioMRI was 0.15 T.

The postoperative MRIs were performed after 3 months.</td>
<td>Moderate</td>
</tr>
<tr>
<td>Wu, 2009, China</td>
<td>Diagnostic study

49 patients with pituitary adenomas

Low-field ioMRI compared with high-field postoperative MRI (as reference method)

No withdrawals or drop-outs</td>
<td><u>Prevalence of residual tumour tissue:</u>
- Sensitivity: 63 %
(95 % CI: 26 – 89)
- Specificity: 98 %
(95 % CI: 86 – 100)</td>
<td>The field strength of the ioMRI was 0.15 T.

The postoperative MRIs were performed within 3 days.</td>
<td>Low</td>
</tr>
</table>

Abbreviation. ioMRI = intraoperative magnetic resonance imaging

Appendix 2

Excluded articles.

PICO 1		
No.	Study	Reason for exclusion
	Claus 2005	Not adequate controls
PICO 2A		
No.	Study	Reason for exclusion
	Nimsky 2004	No postoperative diagnostic examination
PICO 2B		
No.	Study	Reason for exclusion
	Ahn 2008	Inadequate presentation of data

Appendix 3, Search strategy, study selection and references

Question(s) at issue:

Does intraoperative MRI lead to better outcome in patients with intracerebral or pituitary tumours, and does it increase the neurosurgical precision?

PICO

PICO 1
P = Patients with brain tumour (intracerebral or pituitary tumour) subjected to neurosurgery
I = Intraoperative MRI
C =No intraoperative MRI
O = 1) Survival
2) Frequency of reoperations
3) Quality of life
4) Symptom relief
5) Degree of resection
6) Risks/Complications

PICO 2A
P = Patients operated for intracerebral tumours
I = Intraoperative MRI
C = Postoperative MRI within 78 hours
O = Concordance between the methods as evaluated by residual tumour volume (sensitivity/specificity)

PICO 2B
P = Patients operated for pituitary tumours
I = Intraoperative MRI
C = Postoperative MRI within 6 months
O = Concordance between the methods as evaluated by residual tumour volume (sensitivity/specificity)

4a) Search strategy:

PubMed 2009-05-28

neurosurgery OR neurosurgical OR neurosurgical procedures

AND

(MRI-guided) OR (Intraoperative MR-guided) OR (Interventional magnetic resonance) OR (iMR OR ioMRI OR iMRI) OR (Interventional magnetic-resonance-imaging-guided) OR (Intraoperative MR imaging) OR (Interventional MR-guided) OR (Intraoperative mobile magnetic resonance imaging) OR (Interventional magnetic resonance imaging) OR (Intraoperative imaging) OR (High-field magnetic resonance imaging) OR (Intraoperative MRI) OR (Intraoperative magnetic resonance imaging) OR (Intraoperative contrast weighted magnetic resonance imaging) OR (Intraoperative neurophysiological monitoring) OR (Intraoperative neuromonitoring) OR (Intraoperative magnetic resonance scanner) OR (Intraoperative ultra low-field magnetic resonance imaging) OR (Intraoperative low-field MRI)

AND

(Brain tumor resection OR Skull base resection) OR (Brain biopsy OR brain biopsies) OR (Craniotomy OR craniotomies) OR (Supratentorial cavernomas OR Supratentorial cavernous hemangiomas OR supratentorial neoplasms) OR (Transsphenoidal) OR (Intracranial tumors) OR (Glioma OR gliomas) OR (Tumor remnant OR tumor remnants) OR (Brain shift) OR (Cortical stimulation) OR (Astrocytoma OR astrocytomas) OR ((Pituitary AND (adenoma OR adenomas OR macroadenoma OR macroadenomas) OR (pituitary tumor OR pituitary tumors)) OR (Glial tumor OR Glial tumors) OR (Intracranial cyst OR intracranial cysts) OR (Cyst drainage) OR (epilepsy surgery) OR (Ventricular tumor OR Ventricular tumors) OR (DBS OR Deep brain stimulation) OR (Skull base tumor OR skull base tumors) OR (oligodendrogliomas OR oligodendroglioma) OR (meningiomas OR meningioma) OR (glioblastomas OR glioblastoma) OR (dysembryoplastic neuroepithelial tumors OR dysembryoplastic neuroepithelial tumor) OR (brain neoplasms OR Brain tumor OR brain tumors)

Limits: Publication Date from 2003/11/01, English, German, Danish, Norwegian, Swedish

741 results

Search updated 2009-07-02 and 2009-08-24

33 results

Cochrane 2009-08-13

(neurosurgery OR neurosurgical OR neurosurgical procedures)

AND

(MRI-guided) OR (Intraoperative MR-guided) OR (Interventional magnetic resonance) OR (iMR OR ioMRI OR iMRI) OR (Interventional magnetic-resonance-imaging-guided) OR (Intraoperative MR imaging) OR (Interventional MR-guided) OR (Intraoperative mobile magnetic resonance imaging) OR (Interventional magnetic resonance imaging) OR (Intraoperative imaging) OR (High-field magnetic resonance imaging) OR (Intraoperative MRI) OR (Intraoperative magnetic resonance imaging) OR (Intraoperative contrast weighted magnetic resonance imaging) OR (Intraoperative neurophysiological monitoring) OR (Intraoperative neuromonitoring) OR (Intraoperative magnetic resonance scanner) OR (Intraoperative ultra low-field magnetic resonance imaging) OR (Intraoperative low-field MRI)

45 results
Cochrane reviews: 4
Clinical trials: 33
Technology assessments: 3
Economic evaluations: 5

CRD 2009-08-24

intraoperative AND (magnetic resonance OR MRI), publication year 2003-2009

7 results
Dare: **2**
NHS EED: **1**
HTA: **4**

Reference lists

19 results

b) Eligibility criteria

Language:
English, German, Swedish, Norwegian, Danish

Publication date: November 2003-

Study design:
PICO 1

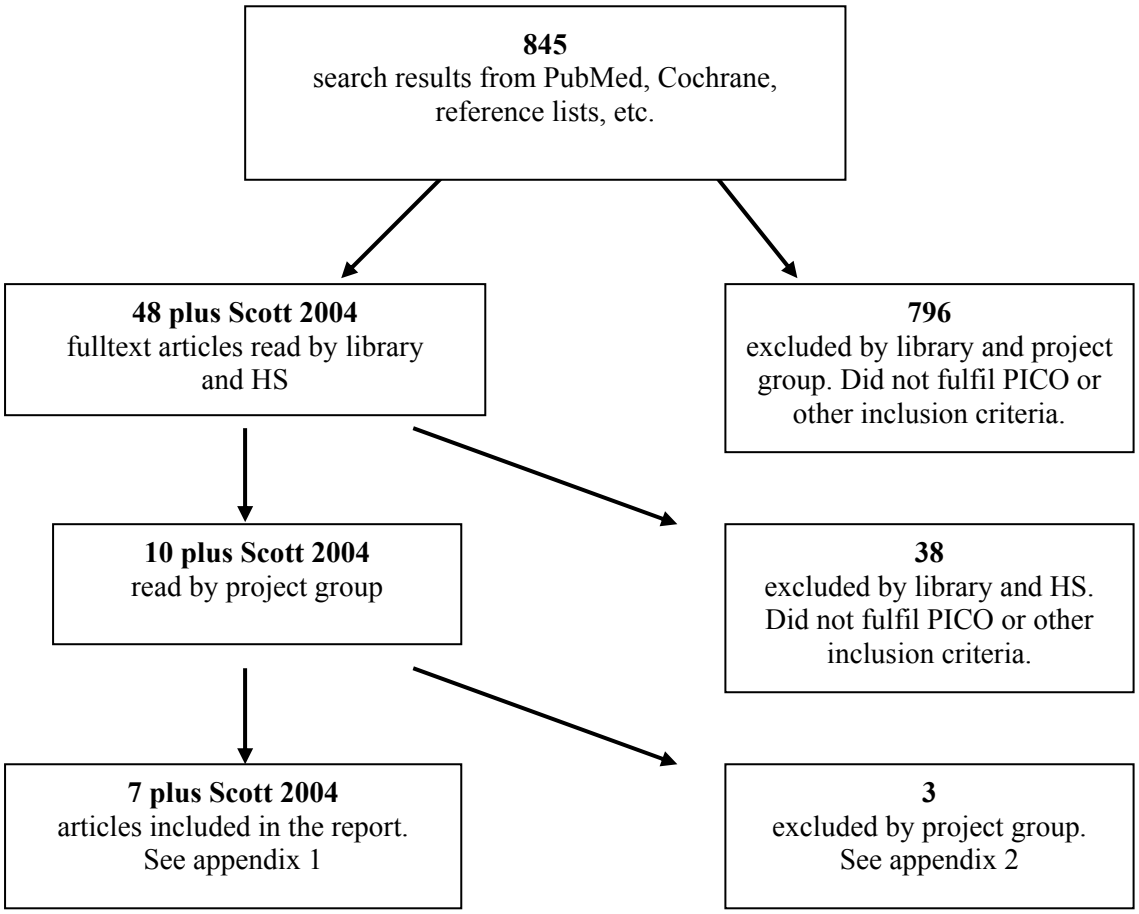
- Studies with some kind of control group
- Case series etc. if ≥ 20 patients. These articles are not critically appraised using check lists, only commented on.
- Systematic reviews

PICO 2A & B

- Studies with some kind of control group
- Case series etc. if ≥ 40 patients. These articles are not critically appraised using check lists, only commented on.
- Systematic reviews

Comment: Since this assessment is based on a Canadian HTA-report published in 2004, the search was done for all studies published after November 2003.

c) Selection process – flow diagram:



d) References:

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Excluded articles:

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VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Sahlgrenska Universitetssjukhuset, HTA-centrum
Röda Stråket 8, 413 45 Göteborg
www.sahlgrenska.se/hta-centrum