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[Intervention Review]

Intraoperative imaging technology to maximise extent of resection for glioma

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ABSTRACT

Background

Extent of resection is considered to be a prognostic factor in neuro-oncology. Intraoperative imaging technologies are designed to help achieve this goal. It is not clear whether any of these sometimes very expensive tools (or their combination) should be recommended as standard care for people with brain tumours. We set out to determine if intraoperative imaging technology offers any advantage in terms of extent of resection over standard surgery and if any one technology was more effective than another.

Objectives

To establish the overall effectiveness and safety of intraoperative imaging technology in resection of glioma. To supplement this review of effects, we also wished to identify cost analyses and economic evaluations as part of a Brief Economic Commentary (BEC).

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 7, 2017), MEDLINE (1946 to June, week 4, 2017), and Embase (1980 to 2017, week 27). We searched the reference lists of all identified studies. We handsearched two journals, the *Journal of Neuro-Oncology* and *Neuro-oncology*, from 1991 to 2017, including all conference abstracts. We contacted neuro-oncologists, trial authors, and manufacturers regarding ongoing and unpublished trials.

Selection criteria

Randomised controlled trials evaluating people of all ages with presumed new or recurrent glial tumours (of any location or histology) from clinical examination and imaging (computed tomography (CT) or magnetic resonance imaging (MRI), or both). Additional imaging modalities (e.g. positron emission tomography, magnetic resonance spectroscopy) were not mandatory. Interventions included intraoperative MRI (iMRI), fluorescence-guided surgery, ultrasound, and neuronavigation (with or without additional image processing, e.g. tractography).

Data collection and analysis

Two review authors independently assessed the search results for relevance, undertook critical appraisal according to known guidelines, and extracted data using a prespecified pro forma.

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Main results

We identified four randomised controlled trials, using different intraoperative imaging technologies: iMRI (2 trials including 58 and 14 participants, respectively); fluorescence-guided surgery with 5-aminolevulinic acid (5-ALA) (1 trial, 322 participants); and neuronavigation (1 trial, 45 participants). We identified one ongoing trial assessing iMRI with a planned sample size of 304 participants for which results are expected to be published around autumn 2018. We identified no trials for ultrasound.

Meta-analysis was not appropriate due to differences in the tumours included (eloquent versus non-eloquent locations) and variations in the image guidance tools used in the control arms (usually selective utilisation of neuronavigation). There were significant concerns regarding risk of bias in all the included studies. All studies included people with high-grade glioma only.

Extent of resection was increased in one trial of iMRI (risk ratio (RR) of incomplete resection 0.13, 95% confidence interval (CI) 0.02 to 0.96; 1 study, 49 participants; very low-quality evidence) and in the trial of 5-ALA (RR of incomplete resection 0.55, 95% CI 0.42 to 0.71; 1 study, 270 participants; low-quality evidence). The other trial assessing iMRI was stopped early after an unplanned interim analysis including 14 participants, therefore the trial provides very low-quality evidence. The trial of neuronavigation provided insufficient data to evaluate the effects on extent of resection.

Reporting of adverse events was incomplete and suggestive of significant reporting bias (very low-quality evidence). Overall, reported events were low in most trials. There was no clear evidence of improvement in overall survival with 5-ALA (hazard ratio 0.83, 95% CI 0.62 to 1.07; 1 study, 270 participants; low-quality evidence). Progression-free survival data were not available in an appropriate format for analysis. Data for quality of life were only available for one study and suffered from significant attrition bias (very low-quality evidence).

Authors' conclusions

Intra-operative imaging technologies, specifically iMRI and 5-ALA, may be of benefit in maximising extent of resection in participants with high grade glioma. However, this is based on low to very low quality evidence, and is therefore very uncertain. The short- and long-term neurological effects are uncertain. Effects of image-guided surgery on overall survival, progression-free survival, and quality of life are unclear. A brief economic commentary found limited economic evidence for the equivocal use of iMRI compared with conventional surgery. In terms of costs, a non-systematic review of economic studies suggested that compared with standard surgery use of image-guided surgery has an uncertain effect on costs and that 5-aminolevulinic acid was more costly. Further research, including studies of ultrasound-guided surgery, is needed.

PLAIN LANGUAGE SUMMARY

Image-guided surgery for brain tumours

Background
Surgery has a key role in the management of many types of brain tumour. Removing as much tumour as possible is very important, as in some types of brain tumour this can help patients to live longer and to feel better. However, removing a brain tumour may in some cases be difficult because the tumour either looks like normal brain tissue or is near brain tissue that is needed for normal functioning. New methods of seeing tumours during surgery have been developed to help surgeons better identify tumour from normal brain tissue.

Question
1. Is image-guided surgery more effective at removing brain tumours than surgery without image guidance?
2. Is one image guidance technology or tool better than another?

Study characteristics
Our search strategy is up to date as of July 2017. We found four trials looking at three different types of tools to help improve the amount of tumour that is removed. The tumour being evaluated was high-grade glioma. Imaging interventions used during surgery included:

• magnetic resonance imaging (iMRI) during surgery to assess the amount of remaining tumour;
• fluorescent dye (5-aminolevulinic acid) to mark out the tumour; or
• imaging before surgery to map out the location of a tumour, which was then used at the time of surgery to guide the surgery (neuronavigation).

All the studies had compromised methods, which could mean their conclusions were biased. Other studies were funded by the manufacturers of the image guidance technology being evaluated.

Key results
We found low- to very low-quality evidence that use of image-guided surgery may result in more of the tumour being removed surgically in some people. The short- and long-term neurological effects are uncertain. We did not have the data to determined whether any of the evaluated technologies affect overall survival, time until disease progression, or quality of life. There was very low-quality evidence for neuronavigation, and we identified no trials for ultrasound guidance. In terms of costs, a non-systematic review of economic studies suggested that compared with standard surgery use of image-guided surgery has an uncertain effect on costs and that 5-aminolevulinic acid was more costly than conventional surgery.

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Quality of the evidence

Evidence for intraoperative imaging technology for use in removing brain tumours is sparse and of low to very low quality. Further research is needed to assess three main questions.

1. Is removing more of the tumour better for the patient in the long term?
2. What are the risks of causing a patient to have worse symptoms by taking out more of the tumour?
3. How does resection affect a patient's quality of life?

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