Preoperative functional MRI use in neurooncology patients: a clinician survey

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OBJECTIVE Functional MRI (fMRI) is increasingly being investigated for use in neurosurgical patient care. In the current study, the authors characterize the clinical use of fMRI by surveying neurosurgeons' use of and attitudes toward fMRI as a surgical planning tool in neurooncology patients.

METHODS A survey was developed to inquire about clinicians' use of and experiences with preoperative fMRI in the neurooncology patient population, including example case images. The survey was distributed to all neurosurgical departments with a residency program in the US.

RESULTS After excluding incomplete surveys and responders that do not use fMRI ($n = 11$), 50 complete responses were included in the final analysis. Responders were predominantly from academic programs (88%), with 20 years or more in practice (40%), with a main area of practice in neurooncology (48%) and treating an adult population (90%). All 50 responders currently use fMRI in neurooncology patients, mostly for low- (94%) and high-grade glioma (82%). The leading decision factors for ordering fMRI were location of mass in dominant hemisphere, location in a functional area, motor symptoms, and aphasia. Across 10 cases, language fMRI yielded the highest interrater reliability agreement (Fleiss' kappa 0.437). The most common reasons for ordering fMRI were to identify language laterality, plan extent of resection, and discuss neurological risks with patients. Clinicians reported that fMRI results were not obtained when ordered a median 10% of the time and were suboptimal a median 27% of the time. Of responders, 70% reported that they had ever resected an fMRI-positive functional site, of whom 77% did so because the site was "cleared" by cortical stimulation. Responders reported disagreement between fMRI and awake surgery 30% of the time. Overall, 98% of responders reported that if results of fMRI and intraoperative mapping disagreed, they would rely on intraoperative mapping.

CONCLUSIONS Although fMRI is increasingly being adopted as a practical preoperative planning tool for brain tumor resection, there remains a substantial degree of discrepancy with regard to its current use and presumed utility. There is a need for further research to evaluate the use of preoperative fMRI in neurooncology patients. As fMRI continues to gain prominence, it will be important for clinicians to collectively share best practices and develop guidelines for the use of fMRI in the preoperative planning phase of brain tumor patients.

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KEYWORDS brain mapping; functional MRI; neurooncology; neurosurgery; clinician survey

FUNCTIONAL MRI (fMRI) has rapidly gained prominence since the first successful fMRI scan was performed in 1991.¹ By imaging the ratio of oxygenated and deoxygenated hemoglobin, T2*-weighted MR images are able to measure changes in cerebral blood flow, a surrogate for neuronal activation. fMRI has enabled visualization of brain activation and expanded our understanding of human brain function in both healthy and diseased

states.⁹ Since its inception as a medical imaging modality, fMRI has attracted significant attention for its potential clinical applications, especially for presurgical mapping.¹²

A large volume of academic research has reported the potential utility of fMRI, including more than 20,000 publications in the first 20 years of its existence.¹² The current body of research has done much to improve imaging hardware, methodology, processing methods, image display

ABBREVIATIONS DTI = diffusion tensor imaging; fMRI = functional MRI; IQR = interquartile range.

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software, and applications of fMRI.^{1,5} These technological advances have contributed to fMRI becoming a useful clinical functional brain-mapping tool, especially for brain tumor patients.^{6,11,13} However, the question remains whether clinical adoption of fMRI has matched this potential.^{12,14} While the clinical adoption of fMRI for epilepsy patients has been examined,³ for neurooncology patients it has not. We therefore set out in the present study to investigate neurosurgeons' clinical adoption of fMRI for preoperative planning in neurooncology patients.

Methods

Study Design

This study was designed as a clinician survey. It was approved and overseen by the Partners IRB (Brigham and Women's Hospital). All clinician participants provided informed consent (see question 1, Supplement 1).

Survey

The survey (Supplement 1) consisted of several sections, including neurosurgeon demographics, patient population, decision factors for ordering fMRI, case studies, intended purpose of ordering fMRI, feasibility of obtaining fMRI results, use of fMRI results, and comparison to other intraoperative brain mapping techniques. A previous survey of fMRI use in epilepsy patients was referenced in this survey design.³

The survey did not use responder identifiers and was made available on Qualtrics (www.qualtrics.com). Questions were organized with logical hierarchy, allowing answers from some key questions to trigger additional questions to appear. The question formats included multiple choice, some with single answer and some with multiple answer, and sliding scale. All questions were optional, and responders could proceed through the survey if they chose to skip questions. The MR images used in the case studies in the survey were de-identified, and their use was approved by the IRB.

Data Collection

The survey was open between September 1, 2018, and February 28, 2019. We emailed invitations to all neurosurgical residency program directors, residency program administrators, and department chiefs in the US. Using a snowball sampling approach,⁷ we requested that these individuals share the survey link with the faculty, fellows, and residents in their departments.

Data Analysis

Results of the survey were downloaded from Qualtrics and manually cleaned before being processed in RStudio (version 1.1.463, RStudio, Inc.). Survey question responses are summarized in frequencies and percentages, or median and interquartile range (IQR), as appropriate. Case studies were used to examine the agreement between neurosurgeons in ordering fMRI testing procedures. The agreement was quantified by means of the Fleiss' kappa statistic.¹⁰ This statistic measures the strength of the interrater reliability between -1 and 1, taking into account

the possibility of agreement due to chance. Based on this statistic, the strength of agreement could be classified into less than chance (< 0), slight (0.01–0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80), and near perfect (0.81–1.00) based on interpretation guidelines set out in the study by Viera and Garrett.¹⁵ The interrater reliability was calculated for the case studies overall, as well as the agreement within specific functional domains and individual cases.

Results

Excluded Responders

A total of 75 survey responses were started, but only 50 responses were completed and used in the final analysis. Of the responders excluded, there were 11 who reported not using fMRI, 7 who did not complete the survey (average progress 40%), 6 who left the complete survey empty, and 1 who did not consent to the survey (Supplement 1, question 1; Fig. 1).

Of those responders who do not use fMRI, their reasons include the following: equipment not available (n = 3), too difficult to perform (n = 2), do not think it can map language function (n = 2), no buy-in from radiology team (n = 2), not sensitive enough (n = 1), not specific enough (n = 1), not a reliable method (n = 1), not needed in my specialty (n = 1), usually not needed (n = 1), and not the decision-maker (n = 1; Fig. 1). Responders were permitted to choose more than one response.

Responder Demographics

Survey responders were predominantly from academic programs (88%), male (86%), with 20 or more years in practice (40%), and with a primary practice in an adult population (90%). Of those who work with a pediatric population, the median youngest age they thought it was possible to use fMRI was 7 years (IQR 6–8 years). All responders have neurooncology as an area of practice, and 48% reported that neurooncology is their main area of practice (Table 1).

Current Use of fMRI

All included responders currently use fMRI in neurooncology patients, most commonly in low-grade (94%) and high-grade gliomas (82%). Responders reported using preoperative fMRI a median of 10 times (IQR 4–25 times) in the past 12 months. Overall, responders use fMRI in neurooncology patients a median of 24% (IQR 9%–41%) of the time, on low-grade gliomas 38% (IQR 15%–54%) of the time, and on high-grade gliomas 30% (IQR 10%–40%) of the time (Table 2).

Decision Factors for Ordering fMRI

Among the 28 clinical and radiographic indicators, responders scored functional location (median 100, IQR 93–100), aphasia (median 89, IQR 75–100), dominant hemisphere (median 82, IQR 76–100), and motor symptoms (median 84, IQR 73–98) as the most important factors that influence their decision to order an fMRI (on a scale from 0–100). Other important decision factors in-

FIG. 1. Flowchart of survey response screening and inclusion. Q1 = question 1.

cluded the following: unilateral tumor with unclear dominance (median 78, IQR 52–86), hemisphere (median 76, IQR 55–90), intention to perform awake surgery (median 65, IQR 46–96), neurological symptoms (median 60, IQR 45–78), sensory symptoms (median 59, IQR 36–78), appearance of infiltration on scan (median 58, IQR 49–79), diffuse versus compact radiographic characteristic (median 55, IQR 20–77), and visual disturbance symptoms (median 53, IQR 2–81; Fig. 2).

Case Studies

The case studies revealed that the overall agreement between neurosurgeons in ordering fMRI testing was fair (Fleiss' $\kappa = 0.300$). The interrater reliability was highest with regard to the ordering of fMRI for language testing (κ

$= 0.437$), whereas it yielded fair agreement with regard to the ordering of sensorimotor ($\kappa = 0.235$) and motor fMRI testing (0.256), and slight agreement for the visual domain ($\kappa = 0.145$). Analysis of the case-level interrater reliability revealed 1 case with moderate agreement, 4 with fair agreement, 4 with slight agreement, and 1 with agreement less than chance (Table 3). Case 8 had the least agreement ($\kappa = -0.009$); this case involved a 62-year-old woman presenting with 2–3 months of gradual personality changes and vision loss, with a large frontal lesion on MRI (see scans in Supplement 1). Case 9 had the most agreement ($\kappa = 0.408$); this case involved a 51-year-old man presenting with 1 week of electric-like shocks, left-foot shaking, and left lower-extremity twitching, with a small posterior parietal lesion on MRI (see scans in Supplement 1).

TABLE 1. Responder demographics and areas of practice

Survey Question	Value
How many years have you been a practicing neurosurgeon (i.e., years since finishing residency)?	
None, still in residency	9 (18)
0–2 yrs	6 (12)
3–5 yrs	7 (14)
6–9 yrs	3 (6)
10–19 yrs	5 (10)
20+ yrs	20 (40)
What is your gender?	
Female	7 (14)
Male	43 (86)
What is your primary patient population?	
Adult	45 (90)
Pediatric	5 (10)
If you work with a pediatric population, what do you feel is the minimum age for which preoperative fMRI can be used?	Median 7 yrs (IQR 6–8 yrs)
Select your area(s) of medical practice	
Academic	44 (88)
Private	2 (4)
Both	3 (6)
Missing	1 (2)
Select all areas of your neurosurgical practice	
Neurooncology	50 (100)
Skull base	31 (62)
Hydrocephalus	23 (46)
Trauma	20 (40)
Spine	17 (34)
Stereotactic and functional (including epilepsy surgery)	16 (32)
Pediatric neurosurgery	10 (20)
Cerebrovascular (including endovascular)	9 (18)
Peripheral nerve	8 (16)
Neurocritical care	7 (14)
What is your main area of specialty in neurosurgery?	
Neurooncology	24 (48)
Skull base	10 (20)
Pediatric neurosurgery	6 (12)
Stereotactic and functional (including epilepsy surgery)	3 (6)
Cerebrovascular (including endovascular)	2 (4)
Spine	2 (4)
Peripheral nerve	0 (0)
Hydrocephalus	0 (0)
Trauma	0 (0)
Neurocritical care	0 (0)
Other/missing	3 (6)

All data given as number (%) unless otherwise indicated.

TABLE 2. Preoperative fMRI use by patient population

Survey Question	Value
On which patients do you use fMRI for surgical planning? (select all that apply)	
Neurooncology	50 (100)
Stereotactic and functional neurosurgery	15 (30)
Cerebrovascular (including endovascular)	5 (10)
Pediatric neurosurgery	5 (10)
Skull base	4 (8)
Peripheral nerve	0 (0)
Spine	0 (0)
Trauma	0 (0)
Hydrocephalus	0 (0)
Do you currently use fMRI for the surgical planning of neurosurgical patients?*	50 (100)
Approximately how many times have you used fMRI for the surgical planning of neurooncology patients in the past 12 months?	Median 10 (IQR 4–25)
For which neurooncology patients do you use preoperative fMRI? (select all that apply)	
Neurooncology patients	50 (100)
Low-grade glioma	47 (94)
High-grade glioma	41 (82)
Meningioma	11 (22)
Metastases	32 (64)
Other benign lesions	23 (46)
Other malignant lesions	20 (40)
How often do you use preoperative fMRI on these patients?†	
Neurooncology patients	24 (9–41)
Low-grade glioma	38 (15–54)
High-grade glioma	30 (10–40)
Meningioma	17 (6–33)
Metastases	19 (9–35)
Other benign lesions	24 (10–37)
Other malignant lesions	16 (9–33)

All data given as number (%) unless otherwise indicated.

* Value for those who answered “yes.”

† Median percentage of the time (IQR).

Intended Purpose for Ordering fMRI

The most common goals for ordering fMRI were to: identify language laterality ($n = 46$, 92%), plan extent of resection ($n = 44$, 88%), and discuss neurological risks with the patient ($n = 43$, 86%). In response to how useful they thought fMRI was for these purposes (scale 0–100), responders rated “identify language laterality” as a median of 79 (IQR 66–94), “planning extent of resection” as 75 (IQR 50–85), and “discussing neurological risks with patients and family” as 78 (IQR 68–97; Fig. 3).

Feasibility of Obtaining fMRI

Respondents reported that when fMRI was ordered, results were not obtained a median of 10% (IQR 8%–19%)

FIG. 2. Boxplot depiction of factors influencing the decision to order fMRI, in response to the question: "Which of the following factors affect your decision to order a preoperative fMRI?" Survey responses were made on a sliding scale of 0–100 (scale from less important to more important). Boxplot represents minimum, first quartile, median, third quartile, and maximum.

TABLE 3. Interrater reliability among neurosurgeons for ordering preoperative fMRI testing in neurooncology patients

Analysis Type	Fleiss' Kappa	Interpretation*
Analysis by fMRI testing domain		
Domain		
Overall	0.300	Fair agreement
Language testing	0.437	Moderate agreement
Motor testing	0.256	Fair agreement
Sensorimotor testing	0.235	Fair agreement
Visual testing	0.145	Slight agreement
Analysis per case		
Case no.		
1	0.208	Fair agreement
2	0.386	Fair agreement
3	0.300	Fair agreement
4	0.032	Slight agreement
5	0.136	Slight agreement
6	0.168	Slight agreement
7	0.244	Fair agreement
8	-0.009	Agreement less than chance
9	0.408	Moderate agreement
10	0.0137	Slight agreement

* The interrater agreement for the consensus labels was calculated using the Fleiss' kappa statistic. The strength of the interrater agreement can be categorized according to this score as less than chance (< 0), slight (0.01–0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80), and near perfect (0.81–0.99), as given by Viera and Garrett.¹⁵

of the time and the results were suboptimal a median of 27% (IQR 16%–35%) of the time. When queried for why adequate fMRI results were unable to be obtained, most respondents reported that either the patient was unable to adequately perform the task (n = 38, 76%), the patient was unable to lie still during the scan (n = 35, 70%), or there was excess head motion during the scan (n = 26, 52%; Table 4).

Use of fMRI Results

Thirty-five responders (70%) reported that they had at some time resected an fMRI-positive functional site. When queried for why they did so, 27 (77%) responded that the site was cleared using direct stimulation, 4 (11%) did not believe anatomically that it was a language area, 7 (20%) that if there was any deficit it would most likely be temporary, and 9 (26%) that the patient was willing to accept a postoperative language deficit. Twenty-nine responders (58%) reported that at some time they opted out of resection due to the results of fMRI (Table 5).

Comparison to Other Brain Mapping Techniques

Of the intraoperative brain mapping options, the greatest portion of respondents is trained in awake surgery (n = 42, 84%), while sensorimotor mapping is the most regularly used (n = 31, 62%). Overall, 49 responders (98%) reported that if the results of fMRI and intraoperative mapping disagreed, they would rely on the intraoperative mapping. On average, respondents reported that 30% (IQR 15%–43%) of the time they found a disagreement between fMRI and awake surgery. While they report that fMRI has

FIG. 3. Boxplot depiction of survey responders' perceived utility of fMRI, in response to the question: "How useful do you think preoperative fMRI is for the following purposes?" Survey responses were made on a sliding scale of 0–100 (scale from less useful to more useful). Boxplot represents minimum, first quartile, median, third quartile, and maximum.

TABLE 4. Feasibility of obtaining fMRI

Survey Question	Value
When you order a preoperative fMRI, approximately how often were results not obtained?	Median 10% (IQR 8%–19%)
When you order a preoperative fMRI, approximately how often were results suboptimal?	Median 27% (IQR 16%–35%)
For what reasons have you been unable to obtain an adequate fMRI? (select all that apply)	
Patient did not understand the instructions	20 (40%)
Patient unable to adequately perform task	38 (76%)
Patient unable to lie still during scan	35 (70%)
Excess head motion during scan	26 (52%)
Patient refused	6 (12%)
Technical problem	12 (24%)
Insurance coverage problem	10 (20%)
Length of time to do testing	13 (26%)
Adverse event	1 (2%)

a strong effect on the decision to perform awake surgery (73%, IQR 53%–81%), fMRI is not a substitute for awake surgery (24%, IQR 2%–38%). Thirty-eight respondents (76%) use diffusion tensor imaging (DTI), of whom 30 (79%) use fMRI to guide the tractography and 18 (47%) use the tractography to guide the interpretation of fMRI results (Table 5).

Discussion

In surveying neurosurgeons about their perceptions and use of preoperative fMRI for neurooncology patients, we found that there is variability between clinicians. This variability extended across the breadth of the study, including which neurooncology patients should undergo preoperative fMRI, which factors influence the decision to order fMRI, which fMRI to order in the case studies, what purposes fMRI is used for, and the utility of fMRI relative to other brain mapping techniques. These results reflect different experiences with and attitudes toward fMRI, all of which are useful for informing the future of this imaging modality as a clinical tool.

TABLE 5. Comparative performance of fMRI

Survey Question	Value
If you have ever resected fMRI-identified, functional positive sites, why did you do so? (select all that apply)	
I have never done this	15 (30)
Total have done so	35 (70)
The area was cleared using direct stimulation	27 (77)
We did not believe anatomically that it was a language area	4 (11)
If there was any deficit, it would most likely be temporary	7 (20)
Patient was willing to accept a postsurgical language deficit	9 (26)
Have you ever opted not to pursue surgical resection due to the results of preoperative fMRI?	29 (58)
If you use intraoperative brain mapping, please select all the techniques that you use (select all that apply)	
I am trained in awake surgery	42 (84)
I regularly perform awake surgery	22 (44)
I am trained in language mapping	36 (72)
I regularly perform language mapping	21 (42)
I am trained in sensorimotor mapping	41 (82)
I regularly perform sensorimotor mapping	31 (62)
When there is disagreement between the results of intraoperative mapping and fMRI, which do you rely on more?	
Rely more on intraoperative mapping	49 (98)
Rely more on fMRI	1 (2)
In patients who underwent both fMRI and awake surgery, approximately how often was there a disagreement between fMRI and awake surgery?	Median 30% (IQR 15%–43%)
In your experience, preoperative fMRI...*	
...results have a strong effect on your decision to do awake surgery	Median 73% (IQR 53%–81%)
...serves as an indication to perform awake surgery	Median 75% (IQR 55%–81%)
...can substitute for awake surgery	Median 24% (IQR 2%–38%)
If you use preoperative fMRI with DTI (diffuse tensor imaging), please select all that apply	
I use fMRI to see the tractography	30 (79)
I use the tractography to guide the fMRI	18 (47)
I do not use DTI	12 (24)

All data given as number (%) unless otherwise indicated.

* Scale 0–100 (0 = strongly disagree, 100 = strongly agree).

Among the survey responders who reported not using fMRI, their reasons included that fMRI is too difficult to perform, that it is not sensitive or specific enough, and that it is not believed to be able to map language function. While this is the first study to quantify neurosurgeons' perspectives on preoperative fMRI for neurooncology patients, this finding is reflected qualitatively in the literature.^{8,14} Given the advances in technology and research that reflect a strong case for clinical use of fMRI,^{11,16} there may be an opportunity to disseminate updated reviews and guidelines.

Among those who do currently use fMRI for neurooncology patients, we found the median use is 10 times in the past 12 months, and it is used on 24% (IQR 9%–41%) of neurooncology patients. So while its use has increased over time, fMRI is still not used in the preoperative planning of most patients. As Rosen and Savoy explored at the 20-year anniversary of fMRI's inception, fMRI has clearly made an impact scientifically, but its impact medically is not yet "world-changing."¹² In comparison to the ubiquitous use of other imaging modalities, fMRI still has some room to grow in its clinical adoption, such as the use of resting state that may allow more patients to be mapped with fMRI.

The variability of clinical and radiographic indications that influence the decision to order preoperative fMRI is illustrated in Fig. 2. While there are few factors on which clinicians strongly agree, one is that functional area is a clinical indication for fMRI. Others, such as memory loss and handedness, present with such variability that the answers ranged across the entire 0–100 scale of importance. Furthermore, the disagreement across fMRI testing domains and case studies, as illustrated in Table 3, reveals some important differences in opinion regarding the clinical application of fMRI. The diverse opinions come from neurosurgeons around the country, practicing in various different settings, and so these findings may be able to open the conversation to what clinical factors should signal the need for fMRI. The discrepancies should be taken into consideration to develop guidelines for best practices surrounding preoperative fMRI testing in neurooncology patients.

Responders differed in their perspectives on what purpose fMRI can serve, but identification of language laterality was the most agreed-upon purpose (92%), and in the case studies, language fMRI testing yielded the highest interrater reliability ($\kappa = 0.437$). These findings concur with the survey study from Benjamin et al., which found that fMRI was most commonly used to identify the dominant language hemisphere in the preoperative planning of epilepsy patients.³ Furthermore, research into this use of fMRI has yielded compelling evidence for the reliable use of fMRI in assessing language laterality.² In fact, language assessment is the only presurgical fMRI guideline published to date by the American Society of Functional Neuroradiology (ASFNR).⁴ The ASFNR 2017 guidelines for presurgical language assessment by means of fMRI provided the first step toward standardizing fMRI data across institutions, and following this success there may be the opportunity to explore other aspects of presurgical fMRI use that are presently subject to interclinician variability.

Interestingly, 70% of responders report having resected an fMRI-positive site at one time or another. Yet, 58% of responders have ever opted out of resection due to fMRI results. On the one hand, these seemingly contradictory results could reflect the significant variation in use and presumed utility across different practices. On the other hand, this dichotomy could reflect both the confidence in fMRI and understanding of its potential shortcomings. Examining this dichotomy could be instrumental for combining fMRI with other modalities for functional mapping and developing guidelines and best practices on a national scale.

Furthermore, 98% of responders said they would rely on the intraoperative mapping results if the results of fMRI and intraoperative mapping disagreed, which indicates that intraoperative mapping remains the perceived gold standard for preoperative neurosurgical planning. Because responders report that there is disagreement between fMRI and awake surgery 30% of the time, further research is needed to understand the nature of these discrepancies. From this clinician survey, we have identified several areas in which further research is needed. Future studies may include patient outcome studies, and quantitative studies correlating fMRI findings with intraoperative mapping findings.

Strengths and Limitations

A few limitations should be mentioned. The majority of responses (88%) came from neurosurgeons working in academic centers. As such, this survey provides limited insight into the use of fMRI for brain tumor resection in nonacademic centers. Although the survey was distributed across various neurosurgical departments in the US, participation remains self-selective. This could have resulted in a nonrepresentative group of responders, which could be biased toward users and those in favor of fMRI. Yet, this survey does provide valuable information on the non-user group as well. Despite the limitations, we believe this study provides valuable insight into the current use and presumed utility of preoperative fMRI for brain tumor resection among neurosurgeons in the US.

Conclusions

In this survey among neurosurgeons, we found a substantial degree of variability in the current use and presumed utility of fMRI for preoperative surgical planning in brain tumor patients. This variation encompasses clinical and radiographic indications for ordering fMRI, functional domains to test in specific case studies, and clinical purposes of using fMRI. In recent years, clinical use of fMRI has increased, and clinicians have gained valuable and varied experiences with fMRI, which can now be leveraged for the collective development of best practices. A crucial next step toward increasing the clinical adoption of fMRI will be to develop a comprehensive set of guidelines that inform where and when to implement fMRI in the preoperative planning of neurooncology surgical patients.

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Disclosures

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Author Contributions

Conception and design: Golby, Senders. Acquisition of data: Stopa. Analysis and interpretation of data: Stopa, Senders. Drafting the article: Stopa, Senders. Critically revising the article: Golby, Broekman, Vangel. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Golby. Statistical analysis: Stopa, Senders, Vangel. Study supervision: Golby, Broekman.

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