

## BRIEF COMMUNICATION

# Preference-based quality-of-life measures for neocortical epilepsy surgery

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### SUMMARY

Critical to decision analysis studies are measures of outcome utilities. In epilepsy surgery the benefit versus risk ratio is of particular interest in neocortical resections. Using the standard gamble, we measured preferences of 30 epilepsy patients for 10 outcome states specific to neocortical epilepsy surgery. Although considered preliminary, the findings suggest that the value of being sei-

zure-free may be greater than that of continued disabling seizures, even if some deficits typical of “eloquent” cortex injury are incurred with surgery. Seizure freedom achieved with polytherapy medical management may be less desirable than that achieved with surgery and monotherapy.

**KEY WORDS:** Epilepsy surgery, Outcomes research, Decision analysis, Quality of life.

Compared to surgery for mesial temporal lobe epilepsy (MTLE), in which clinical value is established (Wiebe et al., 2001), insufficient evidence exists to make a recommendation as to whether patients will benefit from neocortical epilepsy (NE) surgery (Engel et al., 2003). In contrast to MTLE (Choi et al., 2008), both the risks and benefits are less clear for epilepsy surgery in extratemporal and lateral temporal locations. Specifically for NE, risks are greater for overlap with “eloquent” cortex (cortex responsible for primary sensory, motor, and language function); more extensive evaluation is typically required, including additional functional neuroimaging tests and invasive intracranial electrode recordings (Engel, 1996); and seizure-free outcomes are lower (Spencer et al., 2005). Yet, despite these negatives, NE surgery is routinely performed in tertiary epilepsy centers because the alternative—no surgery and a high likelihood of long-term continued disabling seizures—creates a strong motivation to provide a chance at seizure freedom.

This impetus effects an unusual burden on decision making and assessment of effectiveness because so little is known about the actual clinical utility involved in many NE surgery scenarios. The risk–benefit ratio is not clear in resections that may need to involve partial (or even complete) overlap of eloquent cortex in order to obtain the best chance of a seizure-free outcome. This problem applies whether or not accurate cortical mapping is performed due to a relative unreliability of mapping complex motor, sensory, and cognitive brain function with electrocortical stimulation or functional imaging (Hartman & Lesser, 2007). The limited knowledge regarding deficits associated with, and recovery from, pure cortical resection further confounds prediction of outcome utility (Pilcher et al., 1993). Although one might extrapolate from the stroke literature, the validity of such comparison is questionable. As a result, substantial uncertainty remains on both a case-by-case and a general practice level as to whether and when NE surgery should be a course of treatment. The work presented here begins to address this large evidence gap by ascertaining clinical utilities using preference-based, health-related quality-of-life (HRQOL) scores for model health states specific to neocortical surgery outcomes. Ultimately, the effort aims to develop a decision analysis model that determines optimal weighting for parameters that influence whether NE surgery should be recommended.

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## METHODS

Consecutive epilepsy patients seen either in the University of Alabama at Birmingham (UAB) Seizure Monitoring Unit or outpatient clinics were considered for enrollment in the study. The inclusion criteria were age between 18 and 75 years and a definite diagnosis of epilepsy; the only exclusion criterion was presence of cognitive dysfunction that did not allow the patient to comprehend testing concepts. Thirty-five subjects were seen over 6 weeks. Thirty-two subjects met inclusion criteria and were enrolled and completed the assessments under the approval of the UAB Institutional Review Board. Based on this targeted enrollment number, the study was expected to have 80% power to detect a mean difference of 0.10 in the standard gamble score at an  $\alpha = 0.05$ . Two subjects were excluded because it was ultimately determined that they did not understand the testing method. An equal ratio of male and female patients and roughly equal distributions of patients with well-controlled and medically intractable epilepsy were studied. Six patients had previously undergone epilepsy surgery.

We chose the standard gamble (SG) approach over other assessment tools because it has the greatest theoretical grounding in utility theory and has the advantage of incorporating uncertainty into the utility assessment. Time trade-offs have been found to overestimate health state utilities (Van Wijck et al., 1998). At least one study has found a moderate association between SG and other measures of quality of life in epilepsy (Knut, 1998).

Assessment began with a brief training component to determine whether the patient understood the concepts of the standard gamble (SG) testing. In the second component, patients were asked to assess their preferences for two sets of five different theoretical health states possible in the context of an NE surgery vignette (see Appendix S1). The vignette for the SG was adopted from that used in a decision-analysis of MTLE surgery (Choi et al., 2008). Two changes were made to adopt the vignette to NE surgery. First, the types of complications were changed from visual field and memory loss to language and motor/sensory deficits. Second, transient complications were removed, since they did not have an effect on preferences in the MTLE surgery. We made the assumption that similar transient complications associated with NE would also not have an effect. The first five states were predicated on being free of disabling seizures: (1) postsurgery without deficits, (2) postsurgery with nondominant hand motor/sensory deficit, (3) postsurgery with dominant hand motor/sensory deficit, (4) postsurgery with language deficit (expression or comprehension), and (5) medical management alone. The second set of health states were defined by the same conditions but with the premise that disabling seizures were not eliminated.

An important distinction existed between seizure-free states obtained with surgery and with medical management

alone. Based on typical pre- and postsurgical management, most surgery candidates are treated with more than one antiepileptic drug (AED), and seizure-free patients postsurgery are generally on less medication, commonly monotherapy. Therefore, this distinction was included in the vignette.

Analysis was performed by surveying lack of overlap in 95% confidence intervals (CIs) for SG means, then using Student's *t*-test on measure of difference (with unequal variance) between the SG mean scores for health states of interest.

## RESULTS

Table 1 presents the preference-based quality-of-life values for each of the model health states. Patient preferences followed the expectation that language deficit states were considered worse than hand sensory/motor function loss; and nondominant motor/sensory deficits were preferred to those of the dominant hand. Notably, seizure-free state with nondominant hand deficit (HRQOL score = 0.93; CI 0.91–0.96) was preferred to continued seizures without any deficit (0.78; CI 0.70–0.87), mean difference = 0.15 ( $p < 0.005$ ). In addition, seizure freedom on only one AED following surgery (0.98; CI 0.97–0.99) was preferred to seizure-freedom achieved with polytherapy medical management alone (0.89; CI 0.82–0.96), mean difference = 0.10 ( $p < 0.01$ ).

## DISCUSSION

NE surgery poses unique questions about risk and benefit compared to mesial temporal surgery, which has an established clinical value despite a risk of additional memory

**Table 1. Preference-based health-related quality-of-life (HRQOL) measures for neocortical epilepsy surgery outcomes**

	Mean (95% confidence interval), %
Free of disabling seizures	
Medical management <sup>a</sup>	0.89 (0.82–0.96)
Surgery <sup>b</sup>	
No complication	0.98 (0.97–1.0)
Language deficit	0.83 (0.76–0.9)
Dominant hand deficit	0.88 (0.82–0.93)
Nondominant hand deficit	0.93 (0.91–0.96)
Not free of disabling seizures	
Medical management	0.78 (0.70–0.86)
Surgery	
No complication	0.78 (0.70–0.87)
Language deficit	0.71 (0.62–0.80)
Dominant hand deficit	0.77 (0.70–0.84)
Nondominant hand deficit	0.81 (0.74–0.88)

<sup>a</sup>Medical management and all non seizure-free surgery patients maintained on two or more antiseizure medications.

<sup>b</sup>Postsurgical management maintained on only one AED.

deficits and partial visual field loss. Little is known about the risk benefit ratio for NE surgery, which is completely dependent on variable, patient-specific location of epileptogenic tissue responsible for habitual seizures. Furthermore, the epileptogenic tissue may overlap with “eloquent cortex,” generally defined as that which is critical to primary motor/sensory or language function. The burden of handling the unknowns related to risk of *irreversible* neurologic deficits falls mostly on patients and their families. This patient-driven decision making is arguably appropriate given the elective nature of epilepsy surgery. But as such, it is very important for effectiveness studies and clinical trials to have measures of NE surgery outcome utilities that include patient preferences.

Although preliminary, the results are compelling. First, the suggestion that patients may value elimination of seizures over some persistent neurologic deficits should not necessarily be surprising given the unpredictability, relative severity of disability, psychiatric comorbidity, and cumulative risk seizures have on patients’ lives (Gilliam et al., 1997; Friedman & Gilliam, 2009). And yet, as standard-of-care, resections that overlap eloquent cortex are generally considered *verboten* except in cases of catastrophic epilepsy.

Second, these findings support the significance that AED side effects have on patients’ lives (Gilliam et al., 2004). The results appear to reflect patient experience for an increased likelihood of adverse effects from multiple AEDs compared to monotherapy. The impression that more medications equate to more side effects might be safely assumed. However, it is valuable to have the specific distinction between mono- and polytherapy defined, since the main goal of surgery—to achieve seizure freedom—does not include an expectation that the patient should come off all medications. Very often in clinical practice, though, it is a goal of the patient to reduce AEDs as much as possible following surgery.

This study represents pilot data acquisition that has numerous limitations. The small number of subjects allows only modest precision and it precludes subanalysis for disparities between epilepsy types, or cultural and ethnic differences that may exist. In addition, factors such as severity and duration of epilepsy (that take into account adaptation to disease burden) are almost certainly important confounds that influence assessment of risk and benefit for an intervention such as epilepsy surgery. With regard to neurologic deficits that have not actually been experienced, measure of patient preference, even if precise, may not be accurate. Finally, other preference measures that may reflect other important aspects of HRQOL were not used. Therefore, it is emphasized that these data are preliminary and should be corroborated with additional study of various patient groups before and after surgery along with use of other utility instruments. Yet, initial estimates of these utilities provide an important starting point to begin development of decision analysis models.

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## DISCLOSURE

None of the authors has any conflicts of interest to disclose. We confirm that we read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

The authors declare no conflicts of interest.

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## SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Appendix S1.** Health states used for the Standard Gamble testing.

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