Sinonasal Quality of Life Outcomes After Extended Endonasal Approaches to the Skull Base

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Abstract	 Introduction Endoscopic endonasal skull base surgery (EESBS) leads to significant alterations in sinonasal anatomy and physiology. However, there is limited data available on quality of life (QOL) outcomes following EESBS. Methods A retrospective review of patients undergoing EESBS from January 2014 to April 2017 was performed. Records were reviewed for clinical history, operative details, and 22-item Sinonasal Outcomes Test (SNOT-22) scores. Unadjusted and adjusted linear regression models were utilized to compare change in SNOT-22 scores from baseline in patients who underwent a simple sella approach (SA) or an extended beyond sella approach (BSA).
 Keywords quality of life SNOT-22 Sinonasal Outcomes Test skull base surgery endoscopic surgery pituitary 	Results A total of 108 patients were in the SA group, while 61 patients were in the BSA group. SNOT-22 scores were available at baseline and 3 months for 84 patients, while 6-month scores were available for 49 patients. SNOT-22 scores for all patients were not significantly different at 3 months ($p = 0.40$) or at 6 months ($p = 0.58$). Unadjusted linear regression model did not show an association between the type of approach and change in SNOT-22 score at 3 months ($p = 0.07$) and 6 months ($p = 0.28$). Adjusted regression model showed a significant decrease in SNOT-22 score at 3 months ($p = 0.28$). Adjusted regression model showed a significant change in SNOT-22 score at 6 months ($p = 0.22$). Conclusion Patients undergoing EESBS had no significant change in outcomes at 3 and 6 months. A more extensive BSA was not associated with worse QOL outcomes as measured by SNOT-22.

Introduction

Endoscopic endonasal skull base surgery (EESBS) has been associated with decreased overall morbidity and similar outcomes compared with open techniques.^{1–5} However, EESBS can lead to a significant disruption in sinonasal anatomy and physiology, resulting in significant sinonasal morbidity, including nasal crusting, drainage, anosmia, and obstruction.^{6,7} While several quality of life (QOL) measures have been used for skull base surgery patients,^{8–10} the Sinonasal Outcomes Test (SNOT) is arguably the most appropriate instrument to assess sinonasal morbidity. The survey includes

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sinus-specific domains, as well as psychological and sleep domains that assess general health.^{11,12}

Some studies have described QOL outcomes for patients undergoing EESBS specifically for pituitary adenomas.^{8,13–15} Overall, these studies describe an initial nadir in QOL scores postoperatively with significant improvement thereafter and an eventual return to baseline. However, the applications for EESBS have recently expanded beyond pituitary lesions to include transpterygoid, transplanum, transclival, and transethmoid/cribriform approaches for both benign and malignant lesions. Findings from QOL studies in patients undergoing a simple sella approach (SA) cannot be applied to patients undergoing more extensive approaches.

A few studies have reported QOL outcomes for a wider range of tumor types and locations, both benign and malignant, with similar findings. For example, Derousseau et al, utilizing the SNOT-20 survey, found improvement in psychological and sleep outcomes, without improvement in rhinologic QOL, 1 and 2 years following EESBS for sinonasal malignancies.¹⁶ McCoul et al demonstrated a transient deterioration in SNOT-22 scores in the immediate postoperative period, with significantly improved outcomes 6 and 12 months following EESBS for a variety of skull base lesions.¹⁷ Glicksman et al reported improved SNOT-22 scores 3 months postoperatively following endoscopic resection for both benign and malignant lesions, with sustained improvement at 2 years.¹⁸ Pant et al reported significantly improved outcomes at more than 6 months following EESBS compared with the first 3 months using the SNOT-22 for multiple endonasal endoscopic approaches.¹⁹ Similarly, this study aims to evaluate sinonasal QOL outcomes using the SNOT-22 in patients undergoing EESBS at our institution, and to determine if extended beyond sella approaches (BSA) lead to worse QOL outcomes at 3 and 6 months compared with the simple SA.

Methods

Patient Selection

The current study was approved by the Institutional Review Board at Duke University Medical Center. The Duke Enterprise Data Unified Content Explorer was utilized to identify all patients who underwent EESBS between January 1, 2014, and April 30, 2017, at Duke University Hospital. EESBS was considered any surgery that involved an endonasal endoscopic approach for a lesion with gross involvement of the bone of the skull base with or without intracranial involvement. Purely mucosal lesions were not included. Electronic medical records were reviewed for clinical and operative details including age, gender, smoking status, tumor size, tumor type, approach, reconstruction method, and adjuvant radiation. Preoperative and postoperative (3 and 6 months) SNOT-22 scores were collected.

Surgical Technique

The endoscopic approaches were subdivided into a simple SA and BSA. All surgeries were performed by the surgeons at the Duke Skull Base Center, consisting of both otolaryngologists (D.W.J. and R.A.H.) and neurosurgeons (A.R.Z., P.E.F., and P.J.C.).

When both teams were involved, EESBS involved the twosurgeon, four-handed technique. While there was some variation in surgical technique depending on the surgeon, the SA generally consisted of a bilateral sphenoidotomy, removal of the intersinus septum and rostrum, a 1-cm posterior septectomy, and preservation of bilateral rescue flaps. Turbinate resection was left at the discretion of the surgeon. BSA consisted of any approach that included transplanum, transethmoid/cribriform, transclival, transpterygoid, and transmaxillary approaches to the skull base. Reconstructive technique was at the discretion of the surgical team and did not follow any specific algorithm. In general, only Gelfoam was used for cases in which no cerebrospinal fluid (CSF) leak was visualized. For cases with a CSF leak or significantly exposed neurovascular structures, any combination of abdominal fat, lumbar drainage, free mucosal graft, or pedicled nasoseptal flap (NSF) was used. A near-total resection was defined as more than 75% tumor resection and a partial resection was defined as less than 75% total resection of the tumor of interest.

Statistical Analysis

The SNOT-22 score was calculated as a sum of the 22 items on the questionnaire. The rhinologic domain of the SNOT-22 was calculated as the sum of the following six items: need to blow nose, sneezing, runny nose, thick nasal discharge, loss of smell/taste, and nasal blockage. If an incomplete SNOT-22 questionnaire had at least 50% of items completed, item-level missingness was imputed using mean of the completed items. The imputation method was utilized by Hopkins et al when missing data were encountered in their study to validate the SNOT-22 questionnaire,¹¹ and is consistent with studies utilizing other patient-based outcomes measures.²⁰

The primary outcomes were changes in SNOT-22 scores at 3 and 6 months postoperative compared with preoperative. Baseline characteristics were summarized using mean and standard deviation (SD) for continuous variables or frequency and percentage for categorical variables. A two-sample t-test was used to compare the mean difference between two groups for continuous variables, while chi-square or Fisher's exact test was used for categorical variables. Unadjusted and adjusted linear regression models were implemented to investigate the association between the types of endoscopic approach and changes in SNOT-22 scores. The covariates included in the adjusted regression model were age and tumor size as continuous variables and sex, smoking status, radiation history, and use of NSF as binary variables. Patients with missing values in any covariates were excluded from the regression analysis. Analysis was performed in R version 3.4.1 (Vienna, Austria). A *p*-value < 0.05 was considered significant.

Results

The initial search yielded 169 patients who underwent EESBS during the study period, of which 108 (63.9%) patients were in the SA group, while 61 (36.1%) were in the BSA group. Of the 61 BSA patients, 45 patients had a single extended endonasal approach performed (10 transpterygoid, 21 transethmoid/cribriform, 12 transclival, and 2 transplanum), while 14 patients

Table 1 Baselin	ne characteristics	comparing on	ly SA and	BSA

Characteristics	SA (N = 108)	BSA (N = 61)	Total (<i>N</i> = 169)	p-Value
Age at surgery, mean (SD)	55.3 (17.7)	50.8 (17)	53.6 (17.6)	0.11
Female	51 (47.2%)	30 (49.2%)	81 (47.9%)	0.93
Smoker	20 (18.5%)	8 (13.1%)	28 (16.6%)	0.49
Tumor size in cm, mean (SD)	2.3 (1.2)	3.5 (1.7)	2.6 (1.5)	< 0.0001
Middle turbinate resection	•			
Unilateral	20 (18.5%)	17 (27.9%)	37 (21.9%)	0.02
Bilateral	5 (4.6%)	9 (14.8%)	14 (8.3%)	
None	83 (76.9%)	35 (57.4%)	118 (69.8%)	
Tumor resection				
Gross total	63 (65.6%)	33 (89.2%)	96 (72.2%)	0.03
Near total	20 (20.8%)	2 (5.4%)	22 (16.5%)	
Partial	13 (13.5%)	2 (5.4%)	15 (11.3%)	
CSF leak seen during surgery	47 (43.5%)	36 (59.0%)	83 (49.1%)	0.06
Required take back for CSF leak repair	6 (5.6%)	4 (6.6%)	10 (5.9%)	0.75
Revision surgery	19 (17.6%)	9 (14.8%)	28 (16.6%)	0.67
Adjuvant radiation	1 (0.9%)	8 (13.1%)	9 (5.4%)	0.001
Reconstruction				
Nasoseptal flap	21 (19.8%)	19 (31.1%)	40 (24.0%)	0.13
Abdominal fat	41 (60.3%)	5 (12.2%)	46 (42.2%)	< 0.0001
Free mucosal graft	22 (32.4%)	16 (39.0%)	38 (34.9%)	0.62
Lumbar drain	1 (1.5%)	0 (0.0%)	1 (0.9%)	1

Abbreviations: BSA, beyond sella approach; CSF, cerebrospinal fluid; SA, sella approach; SD, standard deviation. *Note*: Italics denote statistical significance (p < 0.05).

had a combination of two approaches, and 2 patients had a combination of three approaches. The demographics of the two study groups are presented in **~ Table 1**. There was no significant difference between the two groups with regard to age, gender, and smoking status. However, tumor size (p < 0.0001), middle turbinate resection (p = 0.02), and the rate of gross total resection were significantly higher (p = 0.03) in the BSA group. Additionally, the need for adjuvant radiation treatment (p = 0.001) was encountered more frequently in the BSA group. With regard to the reconstructive methods, the use of an abdominal fat graft was more common in the SA group (p < 0.001), but there was no significant difference in the use of NSFs, free mucosal grafts, or lumbar drains. Tumor pathologies are described in **~ Table 2**.

Three-Month Outcomes

Within the study cohort of 169 patients, preoperative and 3-month SNOT-22 scores were available for 84(49.7%) patients. The mean SNOT-22 scores of the SA and BSA groups preoperatively were 19.7 (SD 16.5) and 30.1 (SD 20.2), respectively, and at 3 months were 21 (SD 16) and 24 (SD 19.7), respectively. **- Table 3** demonstrates the changes in total SNOT-22 score by approach 3 months after surgery. For these 84 patients, there was no significant difference in total SNOT-22 scores at 3 months compared with baseline, with a mean difference of -1.70 (95% confidence interval [CI] = -5.75, 2.32; p = 0.40).

An unadjusted regression model without covariates demonstrated that there was no significant association between the type of approach (SA vs. BSA) and change in SNOT-22 scores (estimate = -7.4; 95% CI = -15.4, 0.6; p = 0.07). When the SA and BSA groups were compared in an adjusted regression model controlling for age, gender, smoking status, tumor size, radiation history, and NSF reconstruction as confounders, there was a significant decrease in SNOT-22 scores at the 3-month postoperative period for the BSA group (estimate = -9.9; 95% CI = -19.0, -0.8; p = 0.04) (**-Table 4**).

As for the rhinologic domain, patients in the SA group had a greater degree of worsening of scores compared with the BSA group, but this difference was not statistically significant in both the unadjusted (estimate = -1.6; 95% CI = -4.4, 1.3; p = 0.28) and adjusted (estimate = -0.2; 95% CI = -3.6, 3.2; p = 0.90) regression models (**►Tables 5** and **6**).

Six-Month Outcomes

SNOT-22 scores were available for 49 (29.0%) patients at 6 months from surgery within the study cohort of 169 patients. The total SNOT-22 scores preoperatively for the 49 SA and BSA patients were 19.3 (SD 15.9) and 31.7 (SD 21.9), respectively, and at 6 months was 21 (SD 23.2) and 26.2 (SD 21.7), respectively (**► Table 7**). For the total study cohort, there was no significant difference in SNOT-22 scores at 6 months after surgery compared with baseline, with a mean

Table 2 Tumor pathology

Tumor pathology	Ν
Pituitary adenoma	88
Other	16
Meningoencephalocele	11
CSF leak	10
Craniopharyngioma	9
Fibro-osseous lesions	7
Meningioma	6
Chordoma	5
Chondrosarcoma	4
Cholesterol granuloma	4
Adenocarcinoma	4
Squamous cell carcinoma	3
Esthesioblastoma	3
Inverted papilloma	2
Adenoid cystic carcinoma	2
SNUC	1
Melanoma	1

Abbreviations: CSF, cerebrospinal fluid; SNUC, sinonasal undifferentiated carcinoma.

Note: Other includes Rathke's cleft cyst, prolapsed optic chiasm, metastatic pulmonary carcinoid tumor, respiratory epithelial adenomatoid hamartoma, mycetoma, sarcoma, juvenile angiofibroma, and lymphoma.

	SA (N = 50)	BSA (N = 34)	Total (N = 84)	<i>p</i> -Value
Preoperat	ive			
Mean (SD)	19.7 (16.5)	30.1 (20.2)	23.9 (18.7)	0.01
Postopera	tive			
Mean (SD)	21 (16)	24 (19.7)	22.2 (17.5)	0.44
Change				
Mean (SD)	1.3 (17.4)	-6.1 (19.5)	-1.7 (18.5)	0.07

Table 3 SNOT-22 scores by approach at 3 months (n = 84)

Abbreviations: BSA, beyond sella approach; SA, sella approach; SD, standard deviation; SNOT, Sinonasal Outcomes Test. *Note*: Italics denote statistical significance (p < 0.05).

difference of -1.8 (95% CI = -8.41, 4.78; p = 0.58). An unadjusted regression model without covariates showed no association between the type of approach (SA vs. BSA) and changes in SNOT-22 scores (estimate = -7.2; 95% CI = -20.1, 5.6; p = 0.28). An adjusted regression model controlling for the above-mentioned confounders also demonstrated no significant difference between the surgical approaches and the changes in SNOT-22 scores at 6 months following surgery (estimate = -11.2; 95% CI = -28.5, 6.2; p = 0.22) (**-Table 8**). The overall changes in SNOT-22

Table 4 Linear regression examining association betweenapproach and change in SNOT-22 scores at 3 months whilecontrolling for age, sex, smoker, tumor size, radiation, and useof a nasoseptal flap

	Estimate (95% CI)	p-Value
Approach		
SA	Reference	
BSA	-9.9 (-19.0, -0.8)	0.04
Covariates		
Age	-0.2 (-0.4, 0.02)	0.08
Male	-1.5 (-9.8, 6.8)	0.73
Smoker	0.7 (–11.6, 13.1)	0.91
Tumor size	-2.0 (-5.1, 1.1)	0.22
Radiation	22.5 (6.7, 38.3)	0.007
Nasoseptal flap	7.2 (-1.9, 16.3)	0.12

Abbreviations: BSA, beyond sella approach; CI, confidence interval; SA, sella approach; SNOT, Sinonasal Outcomes Test. *Note*: Italics denote statistical significance (p < 0.05).

Table 5 SNOT-22 rhinologic domain scores by approach at 3 months (n = 84)

	SA (N = 50)	BSA (N = 34)	Total (N = 84)	p-Value
Preoperative				
Mean (SD)	3.3 (4.4)	8.2 (6.6)	5.3 (5.8)	0.0001
Postoperative				
Mean (SD)	5.1 (4.7)	8.3 (6.5)	6.4 (5.7)	0.009
Change				
Mean (SD)	1.7 (5.6)	0.1 (7.8)	1.1 (6.6)	0.28

Abbreviations: BSA, beyond sella approach; SA, sella approach; SD, standard deviation; SNOT, Sinonasal Outcomes Test. *Note*: Italics denote statistical significance (p < 0.05).

Table 6 Linear regression examining association between approach and change in rhinologic domain scores at 3 months while controlling for age, sex, smoker, tumor size, radiation, and use of a nasoseptal flap

	Estimate (95% CI)	p-Value
Approach		
SA	Reference	
BSA	-0.2 (-3.6, 3.2)	0.90
Covariates		
Age	-0.1 (-0.2, -0.02)	0.01
Male	1.9 (-1.2, 4.9)	0.24
Smoker	1.1 (-3.5, 5.7)	0.65
Tumor size	-1.8 (-3.0, -0.6)	0.003
Radiation	2.2 (-3.7, 8.0)	0.47
Nasoseptal flap	2.4 (-1.0, 5.8)	0.17

Abbreviations: BSA, beyond sella approach; CI, confidence interval; SA, sella approach.

Note: Italics denote statistical significance (p < 0.05).

Table 7 SNOT-22 scores by approach at 6 months (n = 49)

	SA (N = 25)	BSA (N = 24)	Total (N = 49)	p-Value	
Preoperat	ive				
Mean (SD)	19.3 (15.9)	31.7 (21.9)	25.3 (19.9)	0.03	
Postopera	Postoperative				
Mean (SD)	21 (23.2)	26.2 (21.7)	23.5 (22.4)	0.42	
Change					
Mean (SD)	1.7 (21.4)	-5.5 (24.4)	-1.8 (23)	0.28	

Abbreviations: BSA, beyond sella approach; SA, sella approach; SD, standard deviation; SNOT, Sinonasal Outcomes Test. *Note*: Italics denote statistical significance (p < 0.05).

Table 8 Linear regression examining association between approach and change in SNOT-22 scores at 6 months while controlling for age, sex, smoker, tumor size, radiation, and use of a nasoseptal flap

	Estimate (95% CI)	p-Value
Approach		
SA	Reference	
BSA	-11.2 (-28.5, 6.2)	0.22
Covariates		
Age	-0.2 (-0.7, 0.2)	0.26
Male	-3.6 (-20.1, 12.9)	0.67
Smoker	-9.1 (-41.3, 23.1)	0.58
Tumor size	0.02 (-5.3, 5.3)	1.00
Radiation	20.6 (-5.4, 46.6)	0.13
Nasoseptal flap	3.0 (-16.2, 22.1)	0.76

Abbreviations: BSA, beyond sella approach; CI, confidence interval; SA, sella approach; SNOT, Sinonasal Outcomes Test.

scores for the SA and BSA over the 6-month study period are demonstrated in **Fig. 1**.

As for the rhinologic domain, patients in the SA group had a greater degree of worsening of scores compared with the BSA group, but this difference was not statistically significant in both the unadjusted (estimate = -3.1; 95% CI = -7.6, 1.4; p = 0.19) and adjusted (estimate = -2.7; 95% CI = -8.4, 3.1; p = 0.37) regression models (**-Tables 9** and **10**). The rhinologic domain changes for the SA and BSA over the 6-month study period are demonstrated in **-Fig. 2**.

Discussion

EESBS allows for a minimally invasive approach to the skull base that is associated with less postoperative morbidity and similar outcomes compared with traditional open approaches. The endoscope provides a wide view of the surgical field, which can be broadened with the use of angled telescopes. The extent of resection and oncologic outcomes has been shown not to be compromised. Additionally, patients incur shorter hospital stays and can frequently return to activities of daily life sooner.^{1–5} Despite these benefits, EESBS can potentially cause significant sinonasal morbidity, especially with approaches that go beyond a simple transsellar approach.

The SNOT-22 is a validated and widely used instrument for patients with chronic rhinosinusitis. Due to the inherent similarities between endoscopic sinus and endoscopic skull base surgery, the SNOT-22 has been applied to EESBS. Using the SNOT-22 instrument, our study demonstrates that those undergoing EESBS do not experience significant changes to OOL scores at 3 and 6 months after surgery compared with preoperative scores. This finding is similar to prior reports that show normalization of scores occurring 3 to 12 months following surgery. For example, McCoul et al prospectively assessed SNOT-22 scores for 85 patients undergoing an endoscopic SA in addition to more extended approaches.¹⁷ A univariate analysis of mean SNOT-22 scores was performed over a 1-year postoperative period, with significant worsening in SNOT-22 scores in the early postoperative period and significant improvements noted 1 year after surgery. Also similar to our study, tumor pathology and reconstructive methods did not affect QOL scores.

It is also notable that in our cohort, the patients with malignant lesions were overwhelmingly in the BSA group, since these lesions typically involved the anterior skull base. These patients were also more likely to have received adjuvant radiation. Despite this, we found that changes in SNOT-22 scores in the BSA group did not differ from those of the SA group. This is in contrast to a study by Pant et al, which tracked postoperative SNOT-22 scores in 51 patients undergoing a variety of endonasal approaches including transellar, transplanum, transpterygoid, transcribriform, and transclival.¹⁹ The authors report that those undergoing transsellar approaches versus more extended approaches and those without NSF reconstruction were noted to have better SNOT-22 scores. Our findings are also in contrast to a study by Derousseau et al, which compared QOL outcomes using the SNOT-20 questionnaire in 72 patients undergoing endoscopic surgery for sinonasal malignancies.¹⁶ At 2 years, the authors reported no significant improvements in the overall and rhinologic domain SNOT-20 scores for these patients.

One of the weaknesses of our study is that follow-up does not extend beyond 6 months, and it is possible that the BSA group, which had a higher rate of adjuvant radiation, could have worse QOL outcomes as late effects of radiation appear and recurrences are diagnosed. Additionally, our data show that use of NSF, which was more frequently used in the BSA group, did not result in worse QOL outcomes. This may be due to the small number of patients in each group undergoing NSF reconstruction, leading to inadequate power to detect a significant difference. Therefore, our results surrounding the NSF should be interpreted with caution.

There are some limitations to this study. As mentioned, almost half of the cohort did not have 3-month postoperative SNOT-22 data, and even fewer had 6-month data. One reason for this is that many patients were doing well at their 1 month postoperative visit and further follow-up was not necessary. It is possible that the BSA group, which had a



Fig. 1 Histogram of changes in SNOT-22 scores for SA and BSA groups at 3 and 6 months. BSA, beyond sella approach; SA, sella approach; SNOT, Sinonasal Outcomes Test.

higher rate of adjuvant radiation, could have worse QOL outcomes as late effects of radiation appear. Categorization of various extended endoscopic approaches into an allinclusive BSA group limits investigation of QOL outcomes that may be a unique approach. For example, it is expected that those undergoing a transcribriform approach will have greater olfactory dysfunction compared with those under-

Table 9 SNOT-22 rhinologic domain scores by approach at 6 months (n = 49)

	SA (N = 25)	BSA (N = 24)	Total (N = 49)	p-Value
Preoperat	ive			
Mean (SD)	3.4 (3.8)	10.1 (6.9)	6.7 (6.4)	0.0001
Postopera	itive			
Mean (SD)	5.3 (6.8)	8.9 (6.8)	7 (7)	0.07
Change				
Mean (SD)	1.8 (7.2)	-1.3 (8.8)	0.3 (8.1)	0.19

Abbreviations: BSA, beyond sella approach; SA, sella approach; SD, standard deviation; SNOT, Sinonasal Outcomes Test. *Note*: Italics denote statistical significance (p < 0.05).

going transpterygoid approaches. However, the categorization of extended endoscopic approaches into a single subgroup was necessary due to the limited number of procedures performed per approach during the study period.

Table 10 Linear regression examining association between approach and change in rhinologic domain of SNOT-22 scores at 6 months while controlling for age, sex, smoker, tumor size, radiation, and use of a nasoseptal flap

	Estimate (95% CI)	<i>p</i> -Value
Approach		
SA	Reference	
BSA	-2.7 (-8.4, 3.1)	0.37
Covariates		
Age	-0.2 (-0.3, -0.02)	0.03
Male	0.7 (-4.8, 6.2)	0.80
Smoker	1.8 (-8.9, 12.5)	0.74
Tumor size	-1.3 (-3.1, 0.4)	0.15
Radiation	5.9 (-2.8, 14.5)	0.19
Nasoseptal flap	-0.04 (-6.4, 6.3)	0.99

Abbreviations: BSA, beyond sella approach; CI, confidence interval; SA, sella approach; SNOT, Sinonasal Outcomes Test.



Fig. 2 Histogram of changes in rhinologic domain of SNOT-22 scores for SA and BSA groups at 3 and 6 months. BSA, beyond sella approach; SA, sella approach; SNOT, Sinonasal Outcomes Test.

Conclusion

Patients undergoing an extended endoscopic BSA did not experience diminished sinonasal QOL compared with baseline and compared with patients undergoing a simple SA. These results can be utilized to guide preoperative discussions and patient counseling. Larger studies are needed to evaluate QOL outcomes for specific approaches for specific tumors.

Note

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Conflict of Interest None.

Financial Disclosure No relevant disclosure.

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