# Stuart E. Harrisson, MRCS David Shooman, MRCS Paul L. Grundy, MD, FRCS

Department of Neurosurgery, Wessex Neurological Centre, Southampton University Hospitals Trust, Southampton, United Kingdom

#### Correspondence:

Stuart E. Harrisson, MRCS, Department of Neurosurgery, Wessex Neurological Centre, Southampton University Hospitals Trust, Southampton, SO16 6YD, UK. E-mail: seharrisson@doctors.net.uk

**Received,** July 27, 2010. **Accepted,** April 21, 2011. **Published Online,** July 14, 2011.

Copyright © 2011 by the Congress of Neurological Surgeons

# A Prospective Study of the Safety and Efficacy of Frameless, Pinless Electromagnetic Image-Guided Biopsy of Cerebral Lesions

**BACKGROUND:** In recent years, frameless navigation techniques have been reported to be safe and effective for biopsy of cerebral lesions.

**OBJECTIVE:** To evaluate the safety and efficacy of a technique of frameless, pinless electromagnetic-guided biopsy for brain lesions with the Medtronic Stealth AxiEM.

**METHODS:** Prospective data were collected on consecutive brain biopsies performed by a single surgeon (P.L.G.) with this technology between October 2007 and May 2010. One trajectory was made per lesion with multiple specimens taken for analysis. Outcome measures included measures of accuracy, histological yield, and complication rate.

**RESULTS:** A total of 150 biopsies were performed in 149 patients (84 male and 65 female patients; age range, 19.8-83.8 years). The consultant performed 49 procedures, supervising a trainee in the others. In only 1 case (0.7%) was there nondiagnosis consequent of a registration error and inaccurate trajectory. In 4 other cases (2.7%), no specific diagnosis was established, but abnormal tissue was identified histologically, and postoperative imaging confirmed accurate targeting of these lesions. There were no instances of intracranial hemorrhage or significant morbidity and no deaths directly attributable to the procedure. Four patients (2.7%) died within 30 days of the procedure but not of complications of surgery. One patient suffered a transitory neurological deficit.

**CONCLUSION:** Electromagnetic navigation is proven to be a simple, safe, and effective innovation for frameless and pinless biopsy of cerebral lesions. This technique is time efficient, and elimination of frame placement enhances patient comfort and facilitates the use of local anesthetic technique.

KEY WORDS: Biopsy, Electromagnetic, Frameless, Image-guidance, Pinless

Neurosurgery 70[ONS Suppl 1]:ons29-ons33, 2012

DOI: 10.1227/NEU.0b013e31822d75af

**B** rain and other nervous system cancers accounted for 12 886 deaths in the United States in 2006. There were 17 918 new cases diagnosed (giving an incidence rate of 6.1/100 000).<sup>1</sup>

In 2006, the National Institute for Health and Clinical Excellence issued guidelines on the management of central nervous system tumors in the United Kingdom.<sup>2</sup> Once a diagnosis was indicated on imaging (computed tomography [CT] or magnetic resonance imaging [MRI]), it was recommended that a histological diagnosis

ABBREVIATION: EM, electromagnetic

be made by biopsy or at resection if possible to guide further treatment.

In recent years, frameless navigation techniques have been widely reported to be safe and effective techniques that can be used for biopsy of cerebral lesions. They have numerous advantages over frame-based procedures, in particular, allowing the routine use of preoperative MRI for planning and the ability to plan surgery and image patients in advance, hence saving time.

These techniques can be performed under local anesthetic or general anesthetic; however, many patients find frame placement under local anesthetic to be painful and distressing. Elimination of frame placement would enhance patient comfort,

NEUROSURGERY

VOLUME 70 | OPERATIVE NEUROSURGERY 1 | MARCH 2012 | ons29

reduce surgical time, and facilitate the more widespread use of local anesthetic techniques.

More recently, electromagnetic (EM) technology has been introduced to image-guided neurosurgery initially using flexible stylets to allow ventricular cannulation.<sup>3</sup> We hypothesized that the EM stylet could be placed down a standard side-cutting biopsy cannula, thus allowing tip tracking without frame placement. Since October 2007, we have been using this system exclusively to guide our biopsies of suspected brain tumors.

The aim of our study was to evaluate the safety and efficacy of a novel technique of frameless, pinless EM-guided biopsy for brain lesions with the Medtronic StealthStation AxiEM system. To the best of our knowledge, this is the first report of a surgical series of EM-navigated frameless, pinless biopsies.

## **METHODS**

Data were collected prospectively for all consecutive cases referred for diagnostic biopsy to a single surgeon (P.L.G.) for an intra-axial brain lesion between October 2007 and May 2010. We previously described our strategy for selecting patients for brain biopsy in a prior series of brain biopsies using a different operative technique.<sup>4</sup> As stipulated by National Institute for Health and Clinical Excellence guidelines, all cases were initially discussed in a neurooncology multidisciplinary team meeting.<sup>2</sup> The cases referred were usually suspiciously oncological in nature, and biopsy was advised only when a lesion was considered unresectable, if craniotomy presented too great a risk, or if surgery was contraindicated (eg, lymphoma). None of the patients had lesions that clinical and radiographic data alone could define definitively. No other biopsy techniques were used during this time.

#### **EM-Guided Biopsy Technique**

Clark et al<sup>3</sup> have previously described the method for neuronavigation using a stylet-based entry system for ventricular catheterization. The StealthStation AxiEM Neuronavigation System (Medtronic, Louisville, Colorado) was used in an identical manner. This technology generates a 3-dimensional weak magnetic field that encompasses the head of the patient. Each point in this field can be localized by its own field strength. These signals are then triangulated from trackers on patient reference devices connected to surgical instruments. In our case, we use the EM stylet (which was originally designed for insertion into ventricular catheters for shunt placement) placed into a side-cutting cannula. A direct reference frame is attached to the patient's head with adhesive, and registration of the system usually takes < 1 minute to perform.

The AxiEM navigation stylet fits perfectly into our standard 19-cm side-cutting cannula (Disposable Brain Biopsy Needle Kit DBN-08-19X; Ad-tech Medical Instrument Corp, Racine, Wisconsin). The tip of the stylet is tracked by the navigation system, and this stylet and cannula combination allows "real-time" navigation and tracking of the tip throughout the procedure. The data generated are then contemporaneously merged with the preoperative imaging. This consisted of T1 gadolinium-enhanced MRI for lesions that demonstrated enhancement, with the inclusion of T2-weighted sequences for those that were difficult to define on T1 images. The target site, entry point, and trajectory were planned on the workstation in advance of surgery.

There was no requirement for rigid head fixation, with most patients positioned on a horseshoe headrest. The patient's head was moveable

within the range of the EM field without affecting the accuracy of the biopsy trajectory. This allowed the biopsies to be performed more easily under local anesthetic. Subsequently, supratentorial biopsies were performed with local anesthetic, and posterior fossa lesions were often performed under general anesthetic. Serendipitously, the AxiEM navigation stylet is exactly the length of our side-cutting cannula (length, 19 cm), and the tip sits comfortably at the end of the shaft (see Figure 1). The surgery then proceeded according to the planned burr-hole placement and intralesional trajectory. The stylet and cannula combination consequentially inserts into a screw-on trajectory guide that is then held in place with a 14-mm screw-on burr-hole cover, the base plate of which is screwed onto the cranium (Trajectory Guide Kit 9733066; Medtronic). The trajectory is then aligned, and the guide is locked (see Figure 2). The biopsy needle is then placed into the lesion. One trajectory per lesion was made with multiple specimens taken for analysis and with no intraoperative neuropathology, as we previously reported.<sup>4</sup>

## RESULTS

Between October 2007 and May 2010, a total of 150 biopsies were performed in 149 patients (84 male and 65 female patients; age range, 19.8 to 83.8 years; mean, 58.3 years; median, 59.6 years). The senior consultant performed 49 procedures, supervising the neurosurgical trainee in the remaining 101. Sixty-nine cases (46%) were performed as day cases, and patients were sent home on the day of surgery (after postoperative check imaging).<sup>5</sup> The median length of stay for the series was 1 night (range, 0 to 13 days). It is our standard policy for these patients to have an outpatient biopsy, but some patients were transferred to us for their operation in poor neurological condition or were unable to return home for some other reason (no responsible adult or long geographical distance), and further inpatient care was our responsibility.

A procedure was considered successful if a definitive diagnosis was established. Definitive histology was established for 145 cases (diagnostic yield, 96.7%; see Table 1). With regard to the location



**FIGURE 1.** The 19-cm side-cutting cannula with the electromagnetic stylet in place.

ons30 | VOLUME 70 | OPERATIVE NEUROSURGERY 1 | MARCH 2012



**FIGURE 2.** The burr-hole cover with a trajectory guide and side-cutting cannula in situ.

of the lesions, there were 33 superficial lesions (depth of biopsy < 20 mm from the cortical surface), 112 deep lesions (all lesions biopsied > 20 mm and not wholly contained in the brainstem), and 5 brainstem lesions (lesions wholly in the brainstem).

## **Cases of Nondiagnosis**

In only 1 case (0.7%) was there an inaccuracy resulting in nondiagnosis, most probably caused by a registration error and inaccurate trajectory. The target was clearly missed, which was

TABLE 1. Pathological Diagnosis of 150 Electromagnetic Pinless,   Frameless Biopsied Lesions				
Histological Diagnosis	Cases, n			
Glioblastoma multiforme	76			
Lymphoma	13			
Astrocytoma grade II	12			
Anaplastic astrocytoma	10			
Oligoastrocytoma grade II	9			
Metastases	7			
Other central nervous system conditions	6			
Anaplastic oligodendroglioma and anaplastic oligoastrocytoma	4			
Oligodendroglioma grade II	4			
No diagnosis, diffuse astrocytosis	2			
No diagnosis, target area hit but no diagnosis made	2			
Anaplastic ganglioglioma	1			
Low-grade glioneuronal tumor, World Health Organization grade I	1			
Subependymoma	1			
Meningioma	1			
No diagnosis, missed target	1			

confirmed with postoperative imaging. After this case, we changed our preoperative practice. We postulated that the headphones that were still being used at this point during the preoperative MRI disturbed the anatomic contours of the lateral head, affecting the contour-based tracer registration. This error has not occurred again since the headphones have not been used. The other possible theory (considered less likely in this case) is one that is commonly espoused as a criticism of frameless navigation techniques: Because the actual surgical position is related to the images acquired preoperatively, a progressive error in registration can be observed during intraoperative navigation as a result of brain shift.<sup>6</sup>

In 4 other cases (2.7%), no specific diagnosis was established, but abnormal tissue was identified histologically, and postoperative imaging confirmed accurate targeting of the lesions. The first patient had a partly enhancing and partly necrotic lesion in the left frontal lobe. The patient attended for preoperative imaging and biopsy but had not omitted antiplatelet therapy, delaying the biopsy for 10 days. He had previously been treated with methotrexate. The tissue biopsied came back as abnormal with inflammatory changes consistent with a steroid-treated lymphoma but no conclusive diagnosis. Postoperative imaging revealed significant resolution of the cerebral lesion, which has still not returned 2 years later. The patient has subsequently had ocular lesions for which he has had 4 biopsies, and in June 2010, a diagnosis of diffuse B-cell lymphoma was made. A unique feature of central nervous system lymphoma compared with other brain tumors is its particular sensitivity to corticosteroids.

Another patient had a lesion biopsied while on steroids, which was again considered likely to be primary central nervous system lymphoma on imaging. Postoperative CT scan showed that the biopsy had been taken from the correct area, and the histology was reported as being due to a chronic reactive inflammatory process. A repeat biopsy performed 6 months later confirmed the diagnosis of diffuse large B-cell lymphoma.

The last 2 patients had imaging that revealed a diffusely infiltrating process but with no solid tumor component. Histology from the biopsy was returned as astrocytosis. It was not possible to confirm whether this was a diffusely infiltrating tumor or simply reflective of reactive changes. In both patients, postoperative imaging demonstrated an accurate biopsy track with multiple samples definitely taken from within the lesion. One patient subsequently proceeded to craniotomy and partial lobectomy for diagnosis; histology showed a diffusely infiltrating grade II oligoastrocytoma. The other patient has had serial imaging that has displayed no development in the size or extent of the diffuse white matter changes over 2 years, and the patient has had several follow-up assessments with no further neurological symptoms.

#### Complications

There were 7 cases (4.7%) in which there were intracranial hemorrhages considered significant on postoperative imaging

#### NEUROSURGERY

(defined as hemorrhages that measured > 10 mm in any 1 axis; the largest measured 15 mm). They caused no symptoms, required no treatment (either medical or surgical), and were considered of no clinical significance.<sup>8</sup> There were no deaths directly attributable to the procedure, although 4 patients (2.7%) died within 30 days of the procedure of other conditions.

Of these 4 patients, the first patient had had a normal postoperative CT head scan and was reviewed in our neurosurgery outpatient clinic, as is our standard postoperative management after 7 days, and by the oncology team after 10 days. At both appointments, the patient was asymptomatic with no apparent problems. The histology was disclosed as anaplastic oligodendroglioma, and directed radiotherapy was planned accordingly. Preoperatively, he had a normal performance status. The patient died later on the 11th day of unknown cause with possible hypotheses including a seizure and intracerebral hemorrhage.

The second patient had an unresectable glioblastoma multiforme at presentation that was biopsied. His tumor grew rapidly; therefore, the decision was made to treat him palliatively. The third patient had multiple metastases from malignant melanoma with a poor performance status preoperatively. After biopsy, once the diagnosis was confirmed, he also received palliative care. The final patient had a large glioblastoma multiforme, which was, after confirmation of histology, treated palliatively.

One patient suffered a transitory neurological deficit.

## CONCLUSION

In 1998, Hall<sup>9</sup> published his series of 134 biopsies showing that stereotactic brain biopsy was a safe and effective way of evaluating intracranial lesions. In the same article, he presented a meta-analysis of other studies showing a combined non-diagnosis rate of 9% and a morbidity and mortality rate of 4.2% in a total of 7471 biopsies. More recent studies have published results with nondiagnosis rates of between 0.7% and 10.6% and combined morbidity and mortality rates of 0.8% to 12.1% (Table 2).<sup>4,9-15</sup> Our new study demonstrates that in using an EM frameless, pinless system, a diagnostic rate of 96.7% with no

significant morbidity or mortality resulting from the actual procedure can be achieved.

We recognize there are potential limitations to this system; we have highlighted that although EM technology tracks the catheter/ stylet in real time, it does not track the brain in this dynamic realm, so any anatomic shift in the brain may lead to inaccuracy. The only current methods of true real-time navigation are intraoperative ultrasonography and intraoperative MRI. With intraoperative ultrasonography, because of to the probes currently available, a larger burr hole is often required with this method than with the EM system.<sup>16</sup>

Completely eliminating nondiagnostic biopsies is difficult. The reasons for 4 of our 5 nondiagnosis cases have been discussed previously. Primary central nervous system lymphoma is known to be highly sensitive to steroids; therefore, it is important that patients suspected of having lymphoma are not started on dexamethasone until after the biopsy has been taken.<sup>7</sup> In cases when diffusely infiltrative gliomas without any solid component are suspected or found, it may be necessary to proceed to open biopsy or partial resection to confirm the diagnosis.

The use and application of EM guidance to treat a variety of different neurosurgical conditions have been discussed previously.<sup>17</sup> We propose that image-guided brain biopsy using frameless, pinless EM-guided technology and placing the stylet in a side-cutting biopsy cannula is a safe, effective, and resource-efficient strategy.

It is apparent that probably the most significant benefit is the elimination of a frame or Mayfield clamp. This method facilitates the use of local anesthetic in the majority of cases and enhances patient comfort. It is significantly more time efficient, obviating frame placement and frame-based imaging considerations, and has rapid patient-to-image registration that takes < 1 minute. This study further supports our previous results that intraoperative neuropathology is not necessary with such techniques<sup>4</sup> and that these procedures may routinely be performed safely as day-case surgery.<sup>5</sup>

## Disclosure

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

TABLE 2. Comparison of Morbidity and Mortality in the Present Series With Previous Studies					
Authors and Year of Publication	Cases, n	Nondiagnosis	Morbidity Rate, %	Mortality Rate, %	Combined Morbidity and Mortality Rate, %
Hall, <sup>9</sup> 1998	7471	9	3.5	0.7	4.2
Barnett et al, <sup>10</sup> 1999	218	3.7	2.9	0.9	3.8
Kreth et al, <sup>11</sup> 2001	326	2	3.1	0	3.1
Paleologos et al, <sup>12</sup> 2001	125	2.4	2.4	0.8	3.2
Kim et al, <sup>13</sup> 2003	300	8.3	3.9	0.6	4.5
Aker et al, <sup>14</sup> 2005	130	6	0.8	0	0.8
Dammers et al, <sup>15</sup> 2008	391	10.6	10.6	1.5	12.1
Shooman et al, <sup>4</sup> 2010	134	0.7	0.7	1.5	2.2
Present series	150	3.3	0.7	0	0.7

ons32 | VOLUME 70 | OPERATIVE NEUROSURGERY 1 | MARCH 2012

#### www.neurosurgery-online.com

## REFERENCES

- US Cancer Statistics Working Group. United States Cancer Statistics: 1999-2006 Incidence and Mortality Web-based Report. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; 2010. Available at: http://www.cdc.gov/uscs.
- National Institute for Health and Clinical Excellence. Guidance on Cancer Services: Improving Outcomes for People With Brain and Other CNS Tumours. 2006. Available at: http://www.nice.org.uk.
- Clark S, Sangra M, Hayhurst C, et al. The use of noninvasive electromagnetic neuronavigation for slit ventricle syndrome and complex hydrocephalus in a pediatric population. *J Neurosurg Pediatr.* 2008;2(6):430-434.
- Shooman D, Belli A, Grundy PL. Image-guided frameless stereotactic biopsy without intraoperative neuropathological examination. *J Neurosurg*. 2010;113(2): 170-178.
- Grundy PL, Weidmann C, Bernstein M. Day-case neurosurgery for brain tumours: the early United Kingdom experience. Br J Neurosurg, 2008;22(3):360-367.
- Nimsky C, Ganslandt O, Cerny S, Hastreiter P, Greiner G, Fahlbusch R. Quantification of, visualization of, and compensation for brain shift using intraoperative magnetic resonance imaging. *Neurosurgery*. 2000;47(5):1070-1079.
- Geppert M, Ostertag CB, Seitz G, Kiessling M. Glucocorticoid therapy obscures the diagnosis of cerebral lymphoma. *Acta Neuropathol.* 1990;80(6):629-634.
- Kulkarni AV, Guha A, Lozano A, Bernstein M. Incidence of silent hemorrhage and delayed deterioration after stereotactic brain biopsy. *J Neurosurg.* 1998;89(1): 31-35.
- 9. Hall WA. The safety and efficacy of stereotactic biopsy for intracranial lesions. *Cancer.* 1998;82(9):1749-1755.
- Barnett GH, Miller DW, Weisenberger J. Frameless stereotaxy with scalp-applied fiducial markers for brain biopsy procedures: experience in 218 cases. *J Neurosurg*. 1999;91(4):569-576.
- Kreth FW, Muacevic A, Medele R, Bise K, Meyer T, Reulen HJ. The risk of haemorrhage after image guided stereotactic biopsy of intra-axial brain tumours: a prospective study. *Acta Neurochir (Wien)*. 2001;143(6):539-545.
- Paleologos TS, Dorward NL, Wadley JP, Thomas DG. Clinical validation of true frameless stereotactic biopsy: analysis of the first 125 consecutive cases. *Neurosurgery*. 2001;49(4):830-835.

- Kim JE, Kim DG, Paek SH, Jung HW. Stereotactic biopsy for intracranial lesions: reliability and its impact on the planning of treatment. *Acta Neurochir (Wien)*. 2003;145(7):547-554.
- Aker FV, Hakan T, Karadereler S, Erkan M. Accuracy and diagnostic yield of stereotactic biopsy in the diagnosis of brain masses: comparison of results of biopsy and resected surgical specimens. *Neuropathology*. 2005;25(3):207-213.
- Dammers R, Haitsma IK, Schouten JW, Kros JM, Avezaat CJ, Vincent AJ. Safety and efficacy of frameless and frame-based intracranial biopsy techniques. *Acta Neurochir (Wien)*. 2008;150(1):23-29.
- Whitehead WE, Jea A, Vachhrajani S, Kulkarni AV, Drake JM. Accurate placement of cerebrospinal fluid shunt ventricular catheters with real-time ultrasound guidance in older children without patent fontanelles. *J Neurosurg*. 2007;107(5 suppl):406-410.
- Hayhurst C, Byrne P, Eldridge PR, Mallucci CL. Application of electromagnetic technology to neuronavigation: a revolution in image-guided neurosurgery. *J Neurosurg.* 2009;111(6):1179-1184.

## COMMENT

Arrisson and coauthors describe a frameless, pinless technique of stereotactic biopsy using electromagnetic image guidance. An advantage of this technique is that it can be done under local anesthesia, facilitating day-case surgery. In addition, the biopsy entry and target points can be planned "offline" preoperatively, saving time in the operating room and further improving efficiency. This series demonstrates a diagnostic yield of 96.7% with no intracranial hemorrhage and 1 transient neurological deficit. These data are comparable to those from frame-based procedures and support the use of frameless, minimally invasive electromagnetic guidance rather than time-consuming frame-based biopsies. Although the indications for biopsy rather than resection are becoming increasingly less common, a safe, frameless, rapid biopsy system is a useful tool.

> **Caroline Hayhurst** Wales, United Kingdom