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The Invention and Early History of the N-Localizer for Stereotactic Neurosurgery

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Abstract

Nearly four decades after the invention of the N-localizer, its origin and history remain misunderstood. Some are unaware that a third-year medical student invented this technology. The following *conspectus* accurately chronicles the origin of the N-localizer, presents recently discovered evidence that documents its history, and corrects misconceptions related to its origin and early history.

Categories: Medical Physics, Radiation Oncology, Neurosurgery
Keywords: stereotactic neurosurgery, stereotactic radiosurgery, image guidance, image-guided, computed tomography, magnetic resonance imaging, positron emission tomography (pet), n-localizer, medical imaging, brain imaging

Introduction And Background

The N-localizer (*aka* N-bar) has become an important tool for image-guided stereotactic neurosurgery and radiosurgery. The N-localizer produces two circles and one ellipse in tomographic images obtained via computed tomography (CT), magnetic resonance (MR), or positron emission tomography (PET). The relative spacing between the ellipse and the two circles precisely determines the position of the tomographic section with respect to the N-localizer (Figure *1*) [1-2].

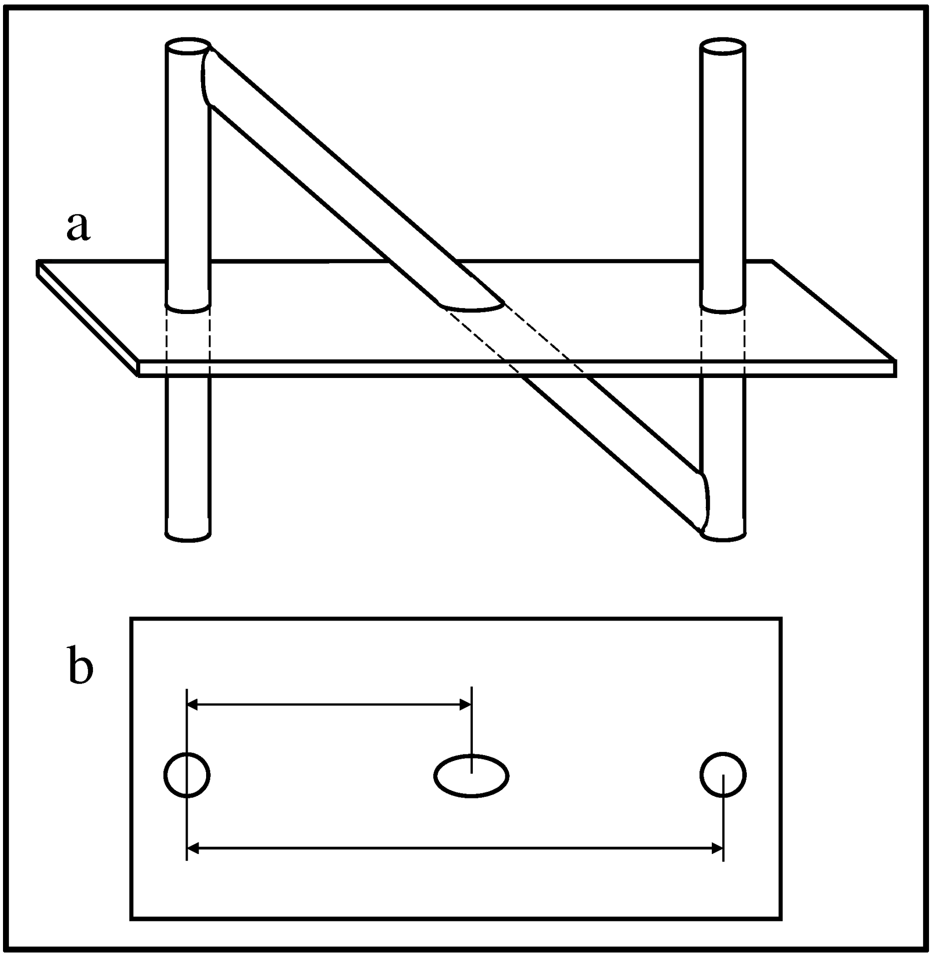

FIGURE 1: N-Localizer and Its Interaction with the Tomographic Section

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(a) Side view of the N-localizer. The tomographic section intersects the N-localizer at two vertical rods and one diagonal rod. (b) Tomographic image. The intersection of the tomographic section with the N-localizer produces two circles and one ellipse. The relative spacing between the centers of the ellipse and the two circles varies according to the height at which the tomographic section intersects the diagonal rod. Measuring this spacing permits calculation of the position of the tomographic section with respect to the N-localizer [2].

Russell A. Brown invented the N-localizer in May 1978 when he was a third-year medical student and during a research elective under the supervision of James A. Nelson at the University of Utah [3]. In August 1978, Brown designed and built the first CT-compatible stereotactic frame in order to test the concept of the N-localizer (Figure *2*). This stereotactic frame was presented at a joint meeting of the Western Neurological Society and the American Academy of Neurological Surgery held in Los Angeles, California in October 1978 [1] and at the INSERM Symposium on Stereotactic Irradiations held in Paris, France in July 1979 [4].

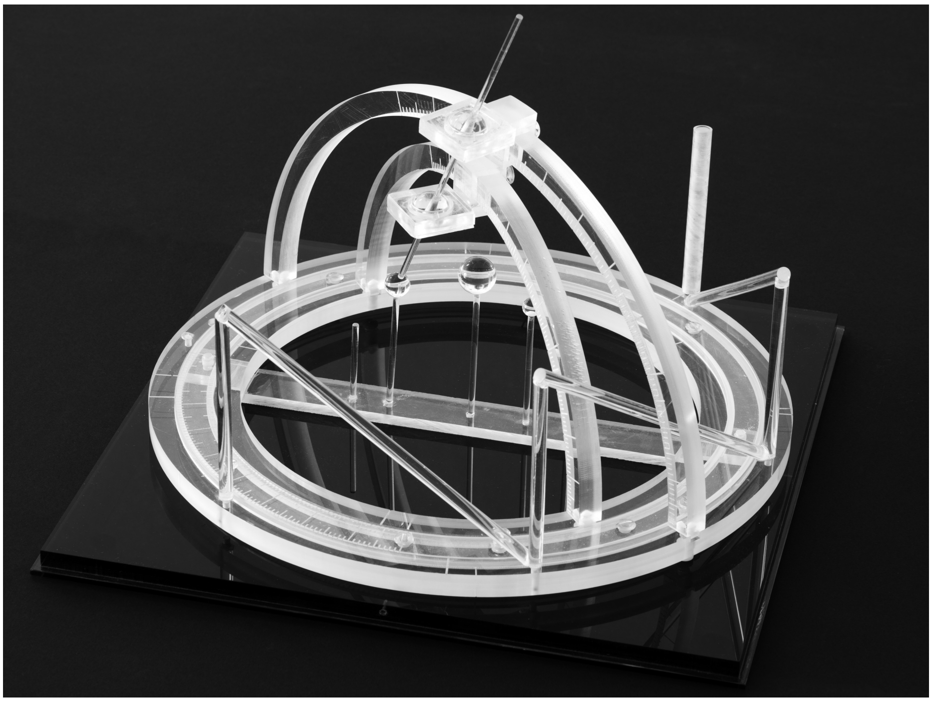


FIGURE 2: The First CT-Compatible Stereotactic Frame

Brown designed and built this stereotactic frame in August 1978 in order to test the concept of the N-localizer [1]. Three N-localizers are attached to this frame and are merged end-to-end such that only seven rods are present. Because three points determine a unique plane in three-dimensional space, the locations of the centers of the three ellipses that the three N-localizers produce in a tomographic image precisely determine the position of the tomographic section with respect to the stereotactic frame [2].

Beginning in 1979, seven different stereotactic frames incorporated the N-localizer: Brown-Roberts-Wells (BRW) [5], Pfizer [6], Todd-Wells [7], Reichert-Mundinger [8-9], Kelly-Goerss Compass [10], Leksell [11], and Cosman-Roberts-Wells (CRW) [12]. Subsequently, the N-localizer achieved widespread use in image-guided stereotactic neurosurgery and radiosurgery directed by CT [13-16], MR [17-21], and PET [22-23].

The N-localizer has assisted stereotactic radiosurgery [24-26] and neurosurgery for tumor biopsy [27-28] and resection [29], for hematoma evacuation [30-31], for cyst and abscess aspiration [31-34], for brachytherapy [31-37], for electrode placement to manage pain [31] and epilepsy [31, 38-39] and to treat Parkinson tremor [40-42], and for thalamotomy, pallidotomy, and dentatomy [31,42]. The simplicity and accuracy of the N-localizer render it an important tool for modern neurosurgery [3].

The impact of the N-localizer on stereotactic surgery and radiosurgery may be estimated from data compiled by Linskey, who counted the types of journal articles published during the years 1966 through 2003 [43]. Those data are summarized as follows [3].

Publications devoted to tumor stereotaxis were a minor fraction of all stereotactic neurosurgery publications until 1979, when the N-localizer was first described [1-2]. Beginning in 1980, the number of publications devoted to stereotactic surgery, brachytherapy or radiosurgery increased rapidly. Publications devoted to frame-based stereotactic surgery dominated until 1994, when they were overtaken by publications devoted to stereotactic radiosurgery. Publications devoted to stereotactic radiosurgery progressively increased and subsequently outnumbered publications devoted to stereotactic surgery or brachytherapy. During the three years from 2001 through 2003, publications devoted to stereotactic radiosurgery comprised roughly two-thirds of all publications devoted to cranial tumor stereotaxis.

The volume of stereotactic radiosurgery assisted by the N-localizer has continued to increase until the present day. Leksell and Lunsford affirm [44], "Statistics reported by about 80% of all Gamma Knife centers indicate that as of 2014, more than a million patients had undergone Gamma Knife surgery, and approximately 60,000 new patients undergo such surgery every year."

Review

During the 38 years since the invention of the N-localizer, misconceptions have arisen concerning its origin and early history in relation to subsequent developments in image-guided stereotactic surgery. Those misconceptions have been discussed previously [45]. The current article presents recently discovered evidence (see Figure *9* in Appendix 6) that corroborates that previous discussion.

The first misconception maintains that the Pfizer frame was the first CT-compatible stereotactic frame and that it was constructed in 1978. Kondziolka and Lunsford of the University of Pittsburgh assert this misconception, together with their failure to discuss the prior literature, in their claim [46], "At our center, the first CT compatible stereotactic head frame, in collaboration with industry, was constructed in 1978 and utilized in 13 patients [6, 47]. *[...]* During this interval, the newly redesigned Leksell CT compatible stereotactic head frame [13] was used for dedicated brain biopsies under the direction of its inventor, Lars Leksell. Several groups were working on devices to allow accurate CT based stereotactic surgery [48]."

The above assertion presents an erroneous chronology. The Pfizer frame was neither the first CT-compatible stereotactic frame (see Figure *2*) nor was it constructed and used in 1978. Instead, it was constructed and used in 1979, as per Lunsford et al., who recount [49], "In 1979, our first efforts in image-guided stereotactic surgery attempted to adapt an early-generation Leksell frame. The metallic artifacts precluded adequate computerized tomography (CT) imaging, and we subsequently developed a CT-compatible stereotactic device (Pfizer frame *[...]*) [50, 6] which was used in an initial series of 15 patients beginning in 1979." This statement is corroborated by Lunsford, Niranjan, Kassam, Khan, Amin, and Kondziolka, who state [51], "During the interval of 1979 to 1980, 13 stereotactic procedures were performed in a diagnostic scanner at our hospital." These two statements confirm that the Pfizer frame was constructed and used in 1979, not in 1978.

Further evidence that the Pfizer frame was constructed in 1979 is provided by Perry, Rosenbaum, Lunsford, Swink, and Zorub, who state [6], "The *Pfizer* stereotactic frame was made after attempts to modify the Leksell frame *[...]* proved difficult" (italics added). This evidence is corroborated by a letter from Perry to Lunsford, Rosenbaum, and Zorub [52] and a letter from Pfizer Medical Systems to its patent attorney [53]. Those letters verify that as of January 15, 1979, Perry, Rosenbaum, Lunsford, and Zorub had not yet attempted any surgery using the modified early-generation Leksell frame. Hence, the Pfizer frame, which was constructed after efforts to adapt the early-generation Leksell frame had failed, was constructed in 1979.

In addition to presenting an erroneous chronology, the above assertion [46] of Kondziolka and Lunsford disregards the fact that the CT-guidance technologies of the Leksell frame and the Pfizer frame were derivative. For both frames, the inclusion of vertical and diagonal elements originated from Brown's prior invention and description of the N-localizer. This fact is established by the articles that introduced the Leksell [13] and Pfizer [6] frames. Both articles cited one [1] of Brown's seminal articles that had introduced the N-localizer one year earlier [1-2]. Although Lunsford (with and without Kondziolka) had previously cited one or the other of Brown's seminal articles in multiple publications [6, 31, 50-51, 54-55], these coauthors cited neither seminal article in their above assertion. Instead, they cited a later article by Roberts and Brown [48] that was published contemporaneously with the first articles from the University of Pittsburgh [6, 47] and one year after Brown's seminal articles had introduced the N-localizer.

The second misconception maintains that investigators from Pfizer Medical Systems and the University of Pittsburgh invented the N-localizer. This misconception is asserted by Lunsford, Niranjan, Kassam, Khan, Amin, and Kondziolka, who claim [51], "During the subsequent years of training, the senior author had an opportunity to work with an innovative neuroradiologist, Arthur Rosenbaum, M.D., and an engineer, John Perry, Ph.D., who then headed the imaging division of Pfizer Medical Instruments. Together, we developed an image-guided stereotactic system using the now well-known N-localizer technology. This elegant solution was proposed by Perry et al. [6] and Rosenbaum et al. [47] independently and virtually simultaneously as publications from Brown [2] and Roberts and Brown [48] of Utah."

In the above assertion, the intended antecedent of "elegant solution" could be "image-guided stereotactic system" or "N-localizer technology." Perry et al. did propose the Pfizer image-guided stereotactic system [6], which incorporated the N-localizer, several months after Brown et al. had proposed the Brown-Roberts-Wells (BRW) image-guided stereotactic system [5]. However, the historical record shows that none of the above-mentioned individuals, with the exception of Brown, invented the N-localizer. Instead, Perry adopted the N-localizer after Brown had disclosed it to him. Documents that corroborate these facts have remained preserved in the archives of the U.S. Patent and Trademark Office for more than 30 years. The following discussion, which is based on those archives, recounts Perry's research related to image-guided stereotactic surgery and reveals the events that led to his adoption of the N-localizer.

Prior to the invention of the N-localizer, Lee, Villafana, and Lapayowker had reported a method for estimating the position of a tomographic section with respect to patient anatomy [56-57]. Their method involved a plate into which were milled vertical slots whose tops lay along a diagonal line (Figure *3*).

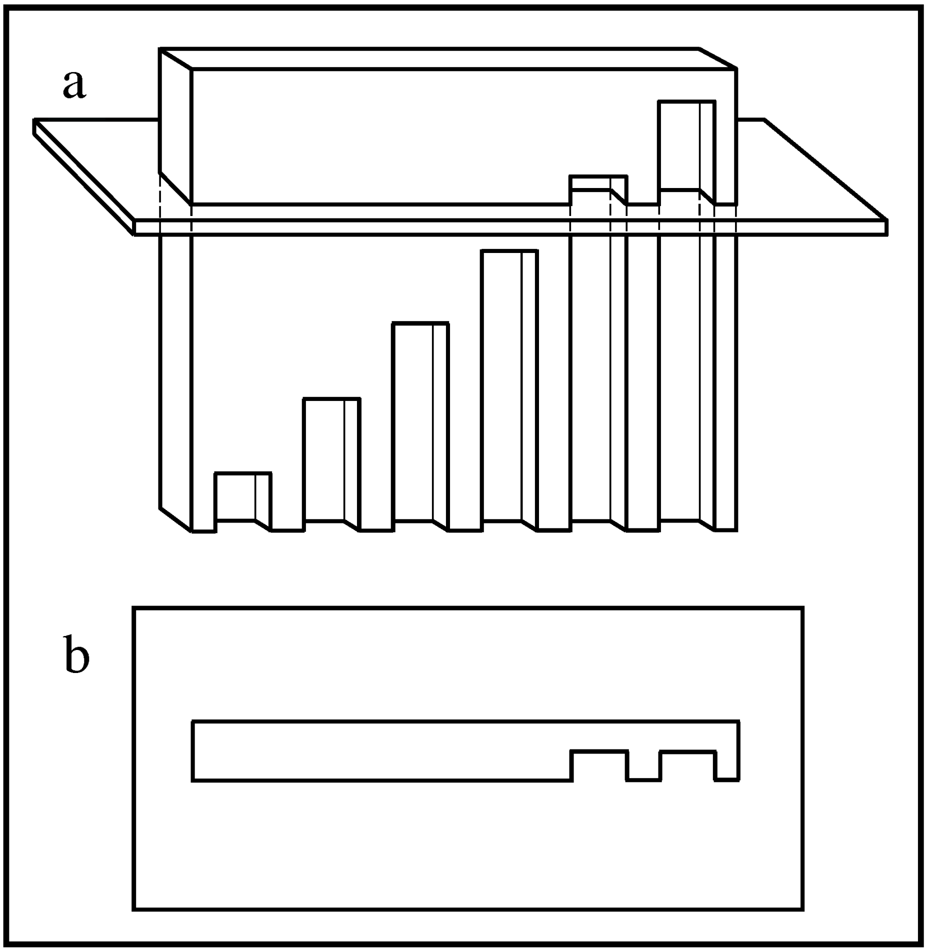


FIGURE 3: Slotted Plate and Its Interaction with the Tomographic Section

(a) Side view of the slotted plate. The tomographic section intersects the plate into which are milled vertical slots of different lengths. The tops of the slots lie along a diagonal line. (b) Tomographic image. The intersection of the tomographic section with the slotted plate produces a variable number of notches. The number of notches depends on the height at which the tomographic section intersects the plate. Counting the number of notches permits estimation of the position of the tomographic section with respect to the slotted plate.

Documents from the archives of the U.S. Patent and Trademark Office indicate that as of January 15, 1979, Perry, Rosenbaum, Lunsford, and Zorub had attached three slotted plates to a Leksell frame [52-53]. In principle, three slotted plates enabled the calculation of the position of a tomographic section with respect to a stereotactic frame, similar to the manner in which three N-localizers enable this calculation (Figure *2*).

In practice, however, the slotted plate was susceptible to error as a result of the discrete or quantized nature of the slots. Perry observed that it was necessary to count carefully the numerous notches that were visible in the tomographic image, because any miscount would give rise to errors in the subsequent calculation of the position of the tomographic section with respect to the stereotactic frame [52]. Moreover, the partial volume effect [58-59], which derives from the several-millimeter thickness of the tomographic section, impeded accurate counting of the notches, because any slot that passed partially into but not entirely through the tomographic section would produce an only faintly visible notch. For these reasons, the slotted plate was vulnerable to human error and hence was unsuitable for clinical use. The N-localizer avoids these quantization problems and the attendant possibility of computational errors by virtue of the continuous nature of the N-localizer's rods.

Perry's earliest description of the slotted plate, and indeed the earliest record of his involvement with image-guided stereotactic surgery, was in his letter dated January 15, 1979, and addressed to his collaborators, Lunsford, Rosenbaum, and Zorub at the University of Pittsburgh [52]. Perry's letter describes three slotted plates attached to a stereotactic frame and provides instructions for using computer software in conjunction with those slotted plates to calculate the position of a tomographic section with respect to that stereotactic frame. Well before the date of Perry's letter, Brown had already invented the N-localizer [60], built the first CT-compatible stereotactic frame [61], and presented his results to the Western Neurological Society and the American Academy of Neurological Surgery [1].

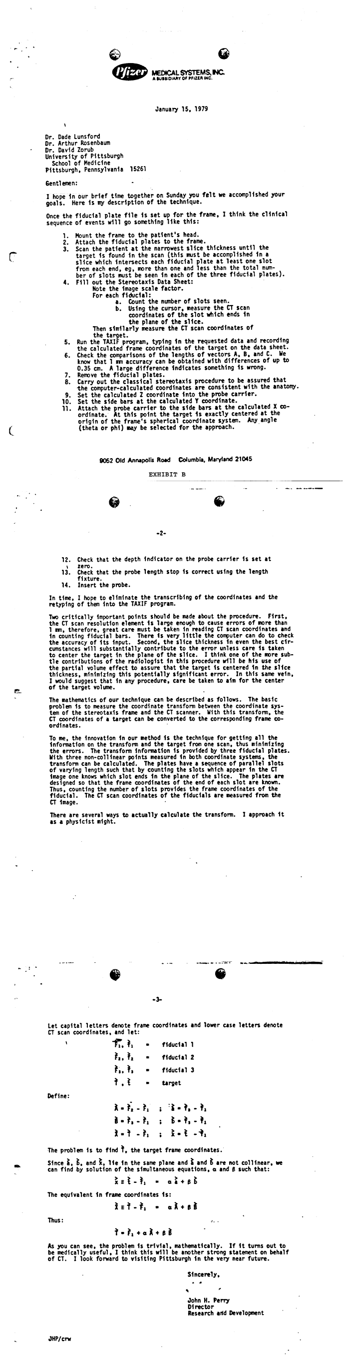
On January 25, 1979, Brown spoke by phone with one of Perry's coworkers at Pfizer Medical Systems and learned that Perry's research concerned image-guided stereotactic surgery [62]. The following day, Pfizer Medical Systems sent to its patent attorney a letter that included a photo of a Leksell frame to which three slotted plates were attached and a photo of a CT image of the Leksell frame and slotted plates [53]. A few days later, Brown spoke by phone with Perry and disclosed the N-localizer to him [63]. Perry et al. subsequently abandoned the slotted plate, adopted the N-localizer, and incorporated it into the Pfizer CT-compatible stereotactic frame [6].

Perry's earliest description of the N-localizer was in his application to the U.S. Patent and Trademark Office dated April 13, 1979 [64]. When challenged by Brown via a Patent Interference proceeding before the U.S. Patent and Trademark Office, Perry failed to provide any evidence whatsoever of having invented the N-localizer. Moreover, Brown's invention of the N-localizer [60] had preceded Perry's earliest involvement with image-guided stereotactic surgery [52] by eight months. Consequently, Perry conceded “priority of invention” to Brown [65], and the U.S. Patent and Trademark Office awarded to Brown patent protection for the N-localizer and for other significant aspects of image-guided stereotactic surgery [66]. The documents [1, 52-53, 60-62, 65] that the U.S. Patent and Trademark Office examined prior to awarding patent protection to Brown instead of Perry are a matter of public record. Those documents may be obtained from the U.S. Patent and Trademark Office by requesting a copy of the folder for Interference No. 101267. In order to facilitate access to those documents, copies are included in the Appendices to this article.

Conclusions

Brown invented the N-localizer and built the first CT-compatible stereotactic frame in 1978. The N-localizer has become an important tool for modern neurosurgery and has achieved widespread use in image-guided stereotactic neurosurgery and radiosurgery directed by CT, MR, and PET. Beginning in 1979, seven different stereotactic frames incorporated the N-localizer. For each frame, the inclusion of the N-localizer was derivative and originated from Brown's research.

Appendices



Pfizer MEDICAL SYSTEMS, INC.
A SUBSIDIARY OF PFIZER INC.

January 15, 1979

Dr. Dade Lunsford
Dr. Arthur Rosenbaum
Dr. David Zorub
University of Pittsburgh
School of Medicine
Pittsburgh, Pennsylvania 15261

Gentlemen:

I hope in our brief time together on Sunday you felt we accomplished your goals. Here is my description of the technique.

Once the fiducial plate file is set up for the frame, I think the clinical sequence of events will go something like this:

1. Mount the frame to the patient's head.
2. Attach the fiducial plates to the frame.
3. Scan the patient at the narrowest slice thickness until the target is found in the scan (this must be accomplished in a slice which intersects each fiducial plate at least one slot from each end, eg, more than one and less than the total number of slots must be seen in each of the three fiducial plates).
4. Fill out the Stereotaxis Data Sheet:
   Note the image scale factor.
   For each fiducial:
   a. Count the number of slots seen.
   b. Using the cursor, measure the CT scan coordinates of the slot which ends in the plane of the slice.
   Then similarly measure the CT scan coordinates of the target.
5. Run the TAXIF program, typing in the requested data and recording the calculated frame coordinates of the target on the data sheet.
6. Check the comparisons of the lengths of vectors A, B, and C. We know that 1 mm accuracy can be obtained with differences of up to 0.35 cm. A large difference indicates something is wrong.
7. Remove the fiducial plates.
8. Carry out the classical stereotaxis procedure to be assured that the computer-calculated coordinates are consistent with the anatomy.
9. Set the calculated Z coordinate into the probe carrier.
10. Set the side bars at the calculated Y coordinate.
11. Attach the probe carrier to the side bars at the calculated X coordinate. At this point the target is exactly centered at the origin of the frame's spherical coordinate system. Any angle (theta or phi) may be selected for the approach.

9052 Old Annapolis Road Columbia, Maryland 21045

EXHIBIT B

-2-

12. Check that the depth indicator on the probe carrier is set at zero.
13. Check that the probe length stop is correct using the length fixture.
14. Insert the probe.

In time, I hope to eliminate the transcribing of the coordinates and the retyping of them into the TAXIF program.

Two critically important points should be made about the procedure. First, the CT scan resolution element is large enough to cause errors of more than 1 mm, therefore, great care must be taken in reading CT scan coordinates and in counting fiducial bars. There is very little the computer can do to check the accuracy of its input. Second, the slice thickness in even the best circumstances will substantially contribute to the error unless care is taken to center the target in the plane of the slice. I think one of the more subtle contributions of the radiologist in this procedure will be his use of the partial volume effect to assure that the target is centered in the slice thickness, minimizing this potentially significant error. In this same vein, I would suggest that in any procedure, care be taken to aim for the center of the target volume.

The mathematics of our technique can be described as follows. The basic problem is to measure the coordinate transform between the coordinate system of the stereotaxis frame and the CT scanner. With this transform, the CT coordinates of a target can be converted to the corresponding frame coordinates.

To me, the innovation in our method is the technique for getting all the information on the transform and the target from one scan, thus minimizing the errors. The transform information is provided by three fiducial plates. With three non-collinear points measured in both coordinate systems, the transform can be calculated. The plates have a sequence of parallel slots of varying length such that by counting the slots which appear in the CT image one knows which slot ends in the plane of the slice. The plates are designed so that the frame coordinates of the end of each slot are known. Thus, counting the number of slots provides the frame coordinates of the fiducial. The CT scan coordinates of the fiducials are measured from the CT image.

There are several ways to actually calculate the transform. I approach it as a physicist might.

-3-

Let capital letters denote frame coordinates and lower case letters denote CT scan coordinates, and let:

$\vec{F}_1, \vec{f}_1$ = fiducial 1

$\vec{F}_2, \vec{f}_2$ = fiducial 2

$\vec{F}_3, \vec{f}_3$ = fiducial 3

$\vec{T}, \vec{t}$ = target

Define:

$$\vec{A} = \vec{F}_2 - \vec{F}_1 \quad ; \quad \vec{a} = \vec{f}_2 - \vec{f}_1$$

$$\vec{B} = \vec{F}_3 - \vec{F}_1 \quad ; \quad \vec{b} = \vec{f}_3 - \vec{f}_1$$

$$\vec{X} = \vec{T} - \vec{F}_1 \quad ; \quad \vec{x} = \vec{t} - \vec{f}_1$$

The problem is to find $\vec{T}$, the target frame coordinates.

Since $\vec{a}$, $\vec{b}$, and $\vec{x}$, lie in the same plane and $\vec{a}$ and $\vec{b}$ are not collinear, we can find by solution of the simultaneous equations, α and β such that:

$$\vec{x} \equiv \vec{t} - \vec{f}_1 = \alpha \vec{a} + \beta \vec{b}$$

The equivalent in frame coordinates is:

$$\vec{X} \equiv \vec{T} - \vec{F}_1 = \alpha \vec{A} + \beta \vec{B}$$

Thus:

$$\vec{T} = \vec{F}_1 + \alpha \vec{A} + \beta \vec{B}$$

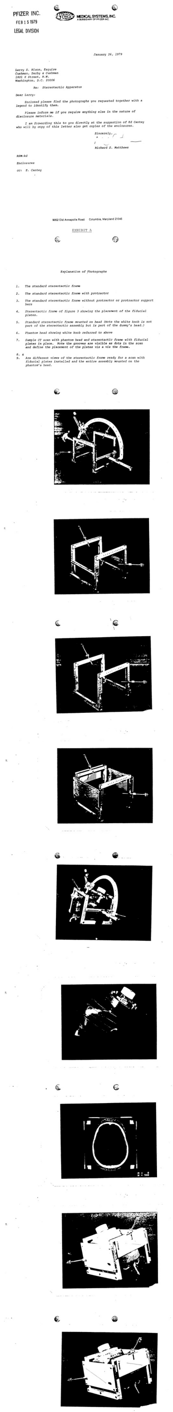
As you can see, the problem is trivial, mathematically. If it turns out to be medically useful, I think this will be another strong statement on behalf of CT. I look forward to visiting Pittsburgh in the very near future.

Sincerely,

John H. Perry
Director
Research and Development

JHP/crw

FIGURE 4: Appendix 1: John Perry Letter, pp. 1-3, January 15, 1979



PFIZER INC.
FEB 15 1979
LEGAL DIVISION

MEDICAL SYSTEMS, INC.
A SUBSIDIARY OF PFIZER INC.

January 26, 1979

Larry S. Nixon, Esquire
Cushman, Darby & Cushman
1801 K Street, N.W.
Washington, D.C. 20006

Re: Stereotactic Apparatus

Dear Larry:

Enclosed please find the photographs you requested together with a legend to identify them.

Please inform me if you require anything else in the nature of disclosure materials.

I am forwarding this to you directly at the suggestion of Ed Cantey who will by copy of this letter also get copies of the enclosures.

Sincerely,

Richard S. Matthews

RSM:kd

Enclosures

cc: E. Cantey

9052 Old Annapolis Road Columbia, Maryland 21045

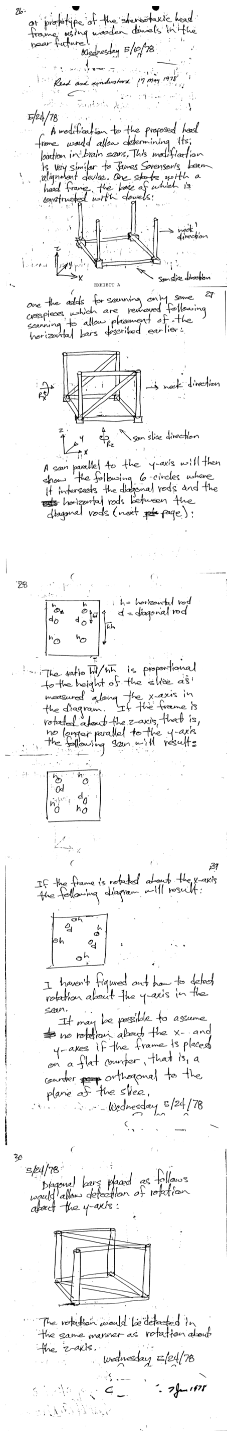
EXHIBIT A

Explanation of Photographs

1. The standard stereotactic frame
2. The standard stereotactic frame with protractor
3. The standard stereotactic frame without protractor or protractor support bars
4. Stereotactic frame of figure 3 showing the placement of the fiducial plates.
5. Standard stereotactic frame mounted on head (Note the white knob is not part of the stereotactic assembly but is part of the dummy's head.)
6. Phantom head showing white knob referred to above
7. Sample CT scan with phantom head and stereotactic frame with fiducial plates in place. Note the grooves are visible as dots in the scan and define the placement of the plates vis a vis the frame.

8. &
9. Are different views of the stereotactic frame ready for a scan with fiducial plates installed and the entire assembly mounted on the phantom's head.

FIGURE 5: Appendix 2: Richard Matthews Letter, pp. 1-7, January 26, 1979



26

or prototype of the stereotaxic head frame using wooden dowels in the near future.

Wednesday 5/10/78

Read and understood 17 May 1978

5/24/78

A modification to the proposed head frame would allow determining its location in brain scans. This modification is very similar to James Sorenson's beam alignment device. One starts with a head frame, the base of which is constructed with dowels:

EXHIBIT A

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one the adds for scanning only some crosspieces which are removed following scanning to allow placement of the horizontal bars described earlier:

A scan parallel to the y-axis will then show the following 6 circles where it intersects the diagonal rods and the horizontal rods between the diagonal rods (next page):

28

The ratio $\overline{hd}/\overline{hh}$ is proportional to the height of the slice as measured along the x-axis in the diagram. If the frame is rotated about the z-axis, that is, no longer parallel to the y-axis the following scan will result:

29

If the frame is rotated about the x-axis the following diagram will result:

I haven't figured out how to detect rotation about the y-axis in the scan.

It may be possible to assume no rotation about the x- and y-axes if the frame is placed on a flat counter, that is, a counter ~~perp~~ orthogonal to the plane of the slice.

Wednesday 5/24/78

30

5/24/78

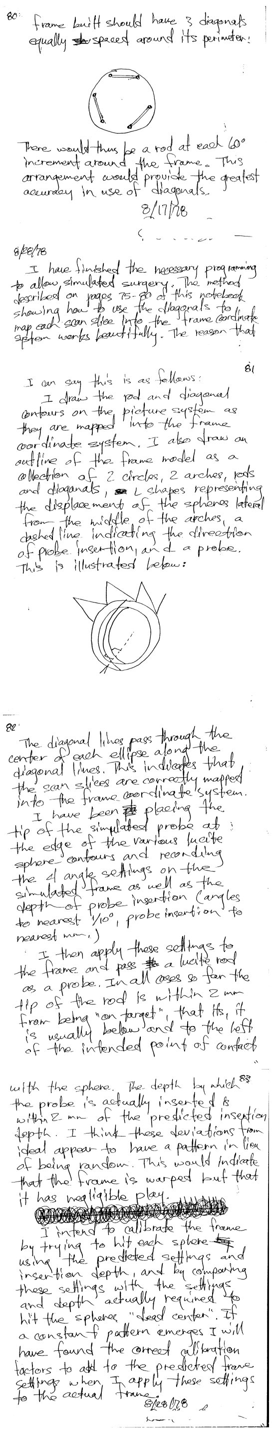
Diagonal bars placed as follows would allow detection of rotation about the y-axis:

The rotation would be detected in the same manner as rotation about the z-axis.

wednesday 5/24/78

7 Jun 1978

FIGURE 6: Appendix 3: Russell Brown Notebook 1, pp. 26-30, May 24, 1978



80 frame built should have 3 diagonals equally spaced around its perimeter:

There would thus be a rod at each 60° increment around the frame. This arrangement would provide the greatest accuracy in use of diagonals.

8/17/78

8/28/78

I have finished the necessary programming to allow simulated surgery. The method described on pages 75-80 of this notebook showing how to use the diagonals to map each scan slice into the frame coordinate system works beautifully. The reason that

81

I can say this is as follows:

I draw the rod and diagonal contours on the picture system as they are mapped into the frame coordinate system. I also draw an outline of the frame model as a collection of 2 circles, 2 arches, rods and diagonals, L shapes representing the displacement of the spheres lateral from the middle of the arches, a dashed line indicating the direction of probe insertion, and a probe. This is illustrated below:

82

The diagonal lines pass through the center of each ellipse along the diagonal lines. This indicates that the scan slices are correctly mapped into the frame coordinate system.

I have been placing the tip of the simulated probe at the edge of the various lucite sphere contours and recording the 4 angle settings on the simulated frame as well as the depth of probe insertion (angles to nearest 1/10°, probe insertion to nearest mm.)

I then apply these settings to the frame and pass a lucite rod as a probe. In all cases so far the tip of the rod is within 2 mm from being "on target", that is, it is usually below and to the left of the intended point of contact

83

with the sphere. The depth by which the probe is actually inserted is within 2 mm of the predicted insertion depth. I think these deviations from ideal appear to have a pattern in lieu of being random. This would indicate that the frame is warped but that it has negligible play.

I intend to calibrate the frame by trying to hit each sphere using the predicted settings and insertion depth, and by comparing these settings with the settings and depth actually required to hit the spheres "dead center". If a constant pattern emerges I will have found the correct calibration factors to add to the predicted frame settings when I apply these settings to the actual frame.

8/28/78

FIGURE 7: Appendix 4: Russell Brown Notebook 1, pp. 80-83, August 28, 1978

54

The square root of the sums of the squares of the three individual errors is taken to be the error for a probe placement. This is possible because these 3 errors are approximately orthogonal to one another. For the 20 probe placements documented on the preceding page the mean error is 2.03 mm and the standard deviation is 0.47 mm.

1/20/79

I was present for a number of these tests, witnessed same, and loaned my hand calculator for calculation of the mean and sigma on 1/20/79

2/8/79

1/25/79

I have spoken with Brian Heightman (sp?) of Pfizer Medical, Inc. about my stereotactic project. He says that John Perry of Pfizer is working on a similar project and has found that the Pfizer reconstruction algorithm is unaffected (or minimally affected) by aluminum. I would, of course, prefer to use aluminum for the frame fabrication because it is more durable than plastic. 1/25/79

FIGURE 8: Appendix 5: Russell Brown Notebook 2, p. 54, January 25, 1979

Pfizer MEDICAL SYSTEMS, INC.
A SUBSIDIARY OF PFIZER INC.

February 2, 1979

Dr. E. Bruce McIff
Utah Valley Hospital
1034 North Fifth Street, West
Provo, Utah 84601

Dear Dr. McIff:

I have spoken with Dr. Russ Brown about his use of your 0200FS scanner for software development relating to stereotaxis. This letter is to assure you that no harm will come to your scanner, provided he observes the following rules:

1. The fixed disk must be write-locked.
2. He must use his own removable disk.

I look forward to seeing the results of this work, and offer my best wishes for success with your 0200FS.

Sincerely,

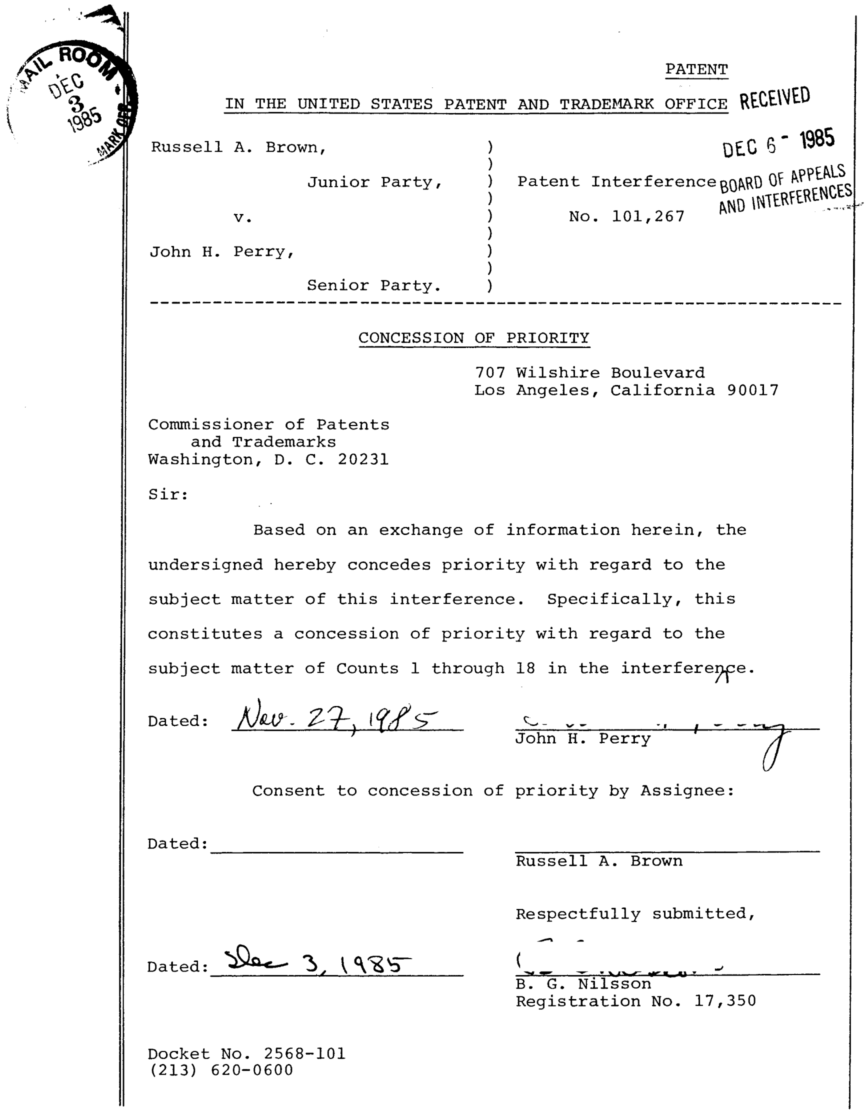
John H. Perry
Research & Development

JHP/cr

cc: Dr. Russ Brown
Mr. Rick Stine

9052 Old Annapolis Road Columbia, Maryland 21045

FIGURE 9: Appendix 6: John Perry Letter, p. 1, February 2, 1979



MAIL ROOM DEC 3 1985

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

RECEIVED DEC 6 - 1985 BOARD OF APPEALS AND INTERFERENCES

Russell A. Brown, Junior Party, v. John H. Perry, Senior Party.

Patent Interference No. 101,267

CONCESSION OF PRIORITY

707 Wilshire Boulevard
Los Angeles, California 90017

Commissioner of Patents
and Trademarks
Washington, D. C. 20231

Sir:

Based on an exchange of information herein, the undersigned hereby concedes priority with regard to the subject matter of this interference. Specifically, this constitutes a concession of priority with regard to the subject matter of Counts 1 through 18 in the interference.

Dated: Nov. 27, 1985 ______ John H. Perry

Consent to concession of priority by Assignee:

Dated: ______ Russell A. Brown

Respectfully submitted,

Dated: Dec 3, 1985 ______ B. G. Nilsson
Registration No. 17,350

Docket No. 2568-101
(213) 620-0600

FIGURE 10: Appendix 7: John Perry Concession of Priority, November 27, 1985

Additional Information

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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