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The Origin of the N-Localizer for Stereotactic Neurosurgery

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Disclosures can be found in Additional Information at the end of the article

Abstract

More than three decades after the invention of the N-localizer, its origin remains misunderstood. Some are unaware that a third-year medical student invented this technology. This historical vignette provides an accurate chronicle of the origin and early history of the N-localizer.

Categories: Medical Physics, Radiation Oncology, Neurosurgery
Keywords: stereotactic radiosurgery, image guidance, stereotactic neurosurgery, computed tomography, magnetic resonance imaging, n-localizer

Introduction And Background

Russell A. Brown invented the N-localizer more than thirty years ago, 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 [1]. Since that time, the N-localizer has achieved widespread use in image-guided stereotactic neurosurgery and radiosurgery. The N-localizer produces two circles and one ellipse in sectional images that are obtained via computed tomography or magnetic resonance imaging (Figure *1*). The relative spacing between the ellipse and the two circles precisely determines the location of the image section relative to the N-localizer [1-2]. The simplicity and accuracy of the N-localizer render it an important tool for modern neurosurgery and radiosurgery. Ironically, however, the accuracy of the N-localizer does not appear to be mirrored by a consistently accurate understanding of its origin.

Lunsford, et al. have claimed [3] that "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. [4] and Rosenbaum, et al. [5] independently and virtually simultaneously as publications from Brown [2] and Roberts and Brown [6] of Utah."

In the preceding statement, the intended antecedent of "elegant solution" could be either "image-guided stereotactic system" or "N-localizer technology". Perry, et al. did propose an image-guided stereotactic system [4] several months after Brown, et al. proposed the Brown-Roberts-Wells (BRW) image-guided stereotactic system [7]. 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 disclosed it to him. The documents that corroborate these facts have remained preserved in the archives of the U.S. Patent and Trademark Office for the past 26 years. The following discussion, which is based on

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these archives, recounts Perry's research related to image-guided stereotactic surgery and reveals the events that led to his adoption of the N-localizer.

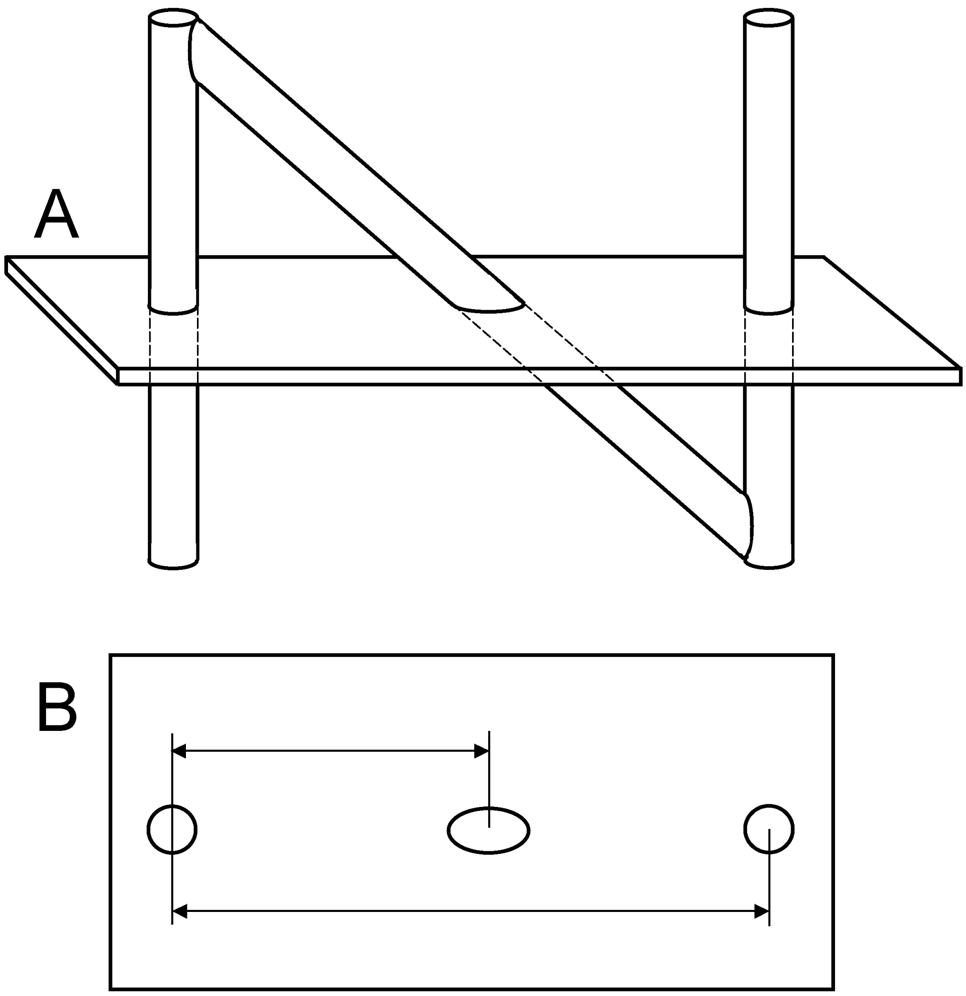


FIGURE 1: N-localizer and its interaction with the computed tomography (CT) scan section

(A) Side view of the N-localizer. The CT scan section intersects two vertical rods and one diagonal rod. (B) CT scan image. The intersection of the CT scan section with the N-localizer produces two circles and one ellipse. The relative spacing between the ellipse and the two circles varies according to the height at which the CT scan section intersects the diagonal rod. Measuring this spacing permits calculation of the location of the CT scan section relative to the N-localizer.

Review

Several researchers had described a method for estimating the position of the computed tomography (CT) scan section [8-9]. This method used a plate into which were milled vertical slots of different lengths, such that the tops of the slots lay along a diagonal line (Figure *2*). The slotted plate produced a variable number of notches in the CT scan image. The number of notches depended on the height at which the CT scan section intersected the plate. Counting the number of notches that were visible in the CT scan image allowed estimation of the location of the CT scan section relative to the slotted plate.

Lunsford discovered that the attachment of two slotted plates to a stereotactic frame permitted determination of the height of the CT scan section relative to the base of the frame [10]. Perry, et al. extended this concept via the attachment of a third slotted plate to the stereotactic frame; the third plate allowed calculation of the orientation of an arbitrarily oriented CT scan section relative to the base of the frame [11]. In principle, this slotted-plate technique that utilized three slotted plates could create the same spatial information that was created by three N-localizers [1-2].

In practice, however, the slotted-plate technique was susceptible to error as a result of the discrete or quantized nature of the slots. Perry observed that it was necessary to manually count carefully the numerous notches that were visible in the CT scan image because any miscount would give rise to errors in the subsequent calculation of the orientation of the CT scan section [11]. Moreover, the partial volume effect [12-13] that derives from the finite thickness of the CT scan section impeded accurate counting of the notches because any slot that passed into but not entirely through the CT scan section could produce an only faintly visible notch. For these reasons, the slotted-plate technique 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.

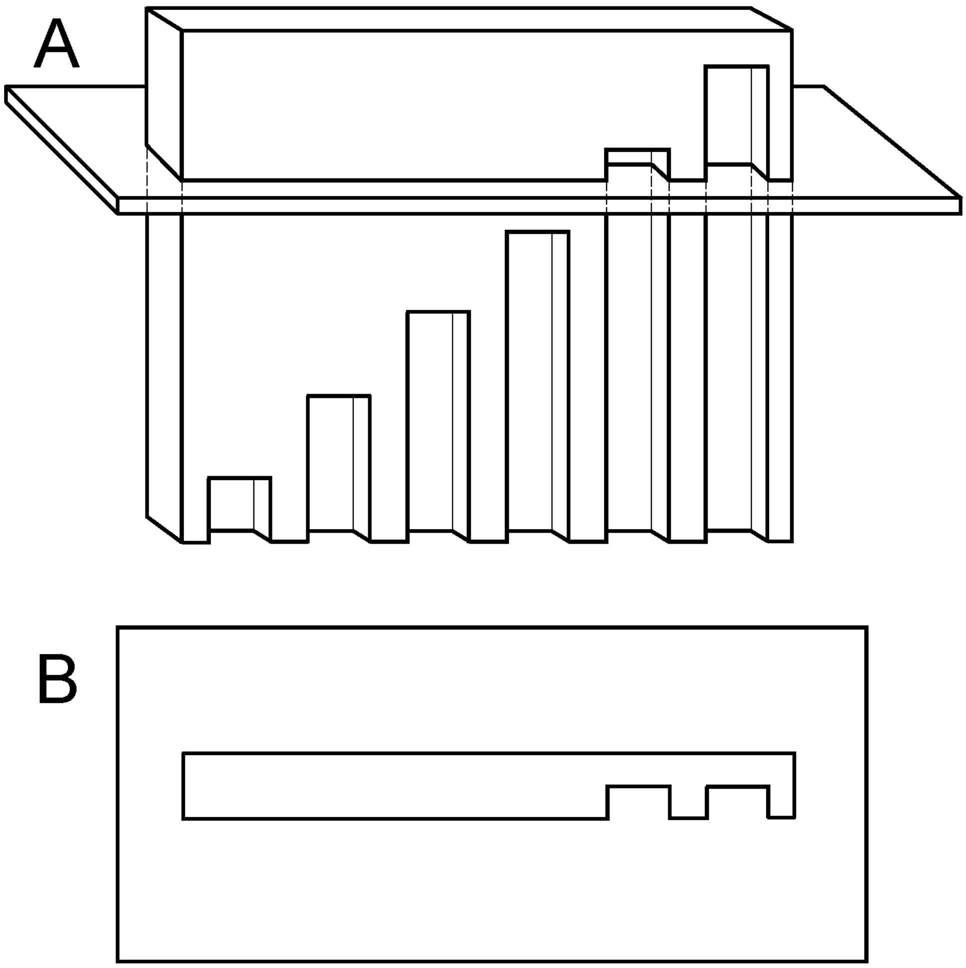


FIGURE 2: Slotted plate and its interaction with the computed tomography (CT) scan section

(A) Side view of the slotted plate. The CT scan section intersects the plate into which are milled vertical slots. The tops of the slots lie along a diagonal line. (B) CT scan image. The intersection of the CT scan section with the slotted plate produces a variable number of notches. The number of notches depends on the height at which the CT scan section intersects the plate. Counting the number of notches permits estimation of the location of the CT scan section relative to the slotted plate.

Perry's earliest report of the slotted-plate technique, and indeed the earliest record of his involvement with image-guided stereotactic surgery, was in his letter dated January 15, 1979 addressed to his collaborators, Dade Lunsford, Arthur Rosenbaum, and David Zorub of the University of Pittsburgh [11]. Perry's letter described the attachment of three slotted plates to a stereotactic frame and provided instructions for using computer software in conjunction with these slotted plates to calculate the spatial orientation of the CT scan section relative to the frame. Well before that date, Brown had already invented the N-localizer [14], built his prototype stereotactic frame [15], and presented his results to the Western Neurological Society and the American Academy of Neurological Surgery [16]. Moreover, on January 29, 1979, Brown submitted for publication the second [2] of his two journal articles that introduced the N-localizer [2, 16].

On January 25, 1979, Brown spoke by phone with one of Perry's coworkers at Pfizer Medical Systems and learned that Perry's research involved image-guided stereotactic surgery [17]. The following day, another of Perry's coworkers at Pfizer Medical Systems sent to a patent attorney a letter that described the slotted-plate technique and that provided several photographs of a stereotactic frame to which three slotted plates were attached [18].

A few days thereafter, Brown spoke by phone with Perry and disclosed the N-localizer to him. Prior to this discussion with Brown, Perry had been unaware of the concept of the N-localizer [19]. Perry may have apprised Rosenbaum of some aspects of this discussion with Brown. Nelson affirms that, during a conversation with Rosenbaum concerning the N-localizer, Rosenbaum revealed his awareness of Brown's previous discussion with Perry [19].

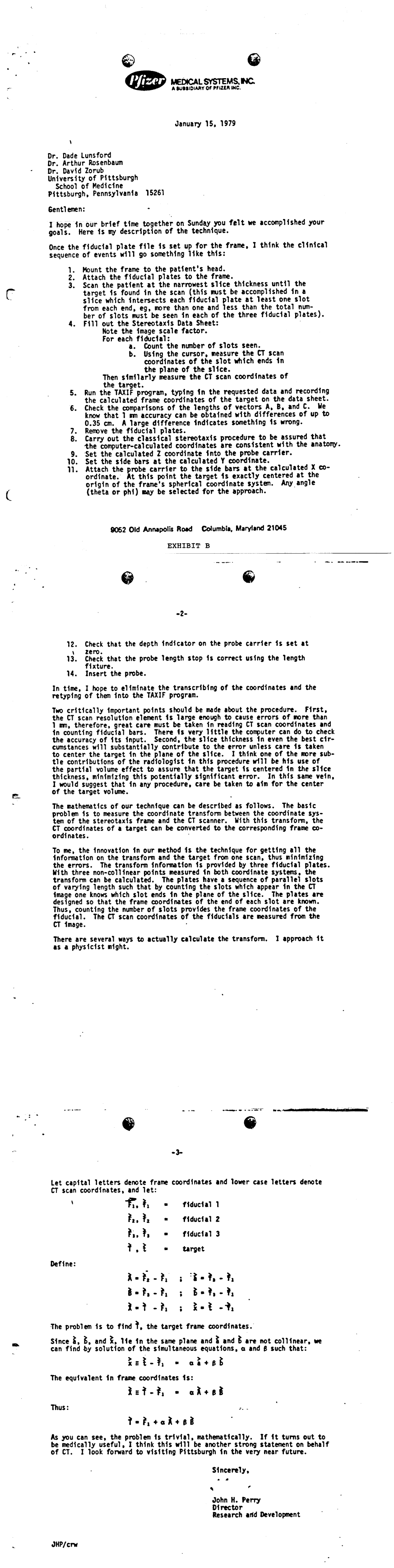
Several months following his discussion with Perry, Brown was surprised to witness a talk wherein Perry presented the N-localizer [19]. When Perry, et al. subsequently proposed an image-guided stereotactic system that comprised N-localizers instead of slotted plates [4], they cited one [16] of Brown's two journal articles that had introduced the N-localizer more than one year previously [2, 16]. Several months before Perry, et al. proposed their image-guided stereotactic system, Brown, et al. had already proposed the BRW image-guided stereotactic system [7].

Perry's earliest description of the N-localizer was cursory and limited to only two sentences in his application to the U.S. Patent and Trademark Office dated April 13, 1979; this same patent application devoted detailed explanations and five drawings to a thorough description of the slotted-plate technique [20]. Upon challenge by Brown, Perry failed to provide any evidence whatsoever of having invented the N-localizer. Consequently, Perry conceded “priority of invention” to Brown [21], and the Patent Office awarded patent protection for the N-localizer to Brown [22]. The documents [11, 14-18, 21] that the Patent Office examined prior to awarding patent protection to Brown instead of Perry are a matter of public record. These documents may be obtained from the patent office by requesting a copy of the folder for Interference No. 101267. In order to facilitate access to these documents, we have included copies in the appendices (labeled as "figures") to this paper.

Conclusions

Brown invented the N-localizer that has become an important neurosurgical tool and has achieved widespread use in image-guided stereotactic neurosurgery and radiosurgery. Lunsford invented the attachment of two slotted plates to a stereotactic frame. Perry, et al. extended this concept via the attachment of a third slotted plate, but the slotted-plate technique never achieved clinical use [23]. Perry abandoned the slotted plate and adopted instead the N-localizer after Brown disclosed it to him. Several months after Brown, et al. proposed the BRW image-guided stereotactic system that comprised N-localizers, Perry, et al. proposed an image-guided stereotactic system that also comprised N-localizers. However, Perry's inclusion of the N-localizer in an image-guided stereotactic system did not occur independently of Brown's discovery of the N-localizer. To the contrary, Perry's inclusion of the N-localizer was derivative; it originated from Brown's prior research. The historical documents that confirm these facts are a matter of public record and remain accessible at the archives of the U.S. Patent and Trademark Office.

Appendices



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.

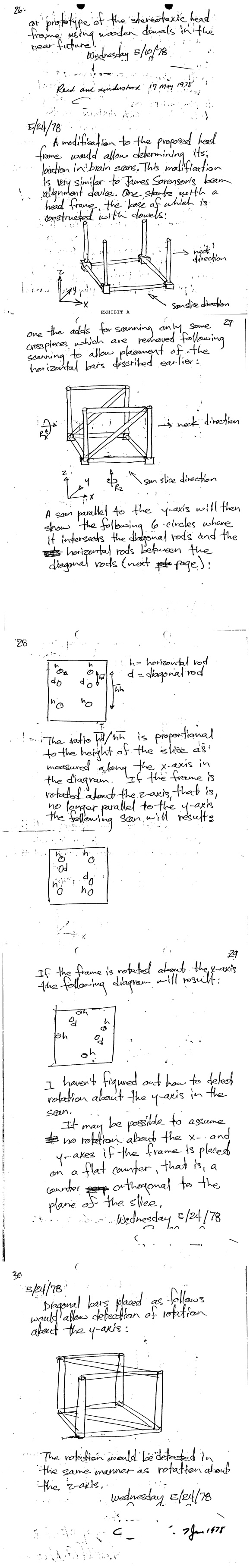
Sincerely,

John H. Perry
Director
Research and Development

JHP/crw

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

1979



26.

a 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 Sorensen's beam alignment device. One starts with a head frame, the base of which is constructed with dowels:

27

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

h = horizontal rod
d = diagonal rod

The ratio ... 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 orthogonal to the plane of the slice.

Wednesday 5/24/78

30

5/31/78

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

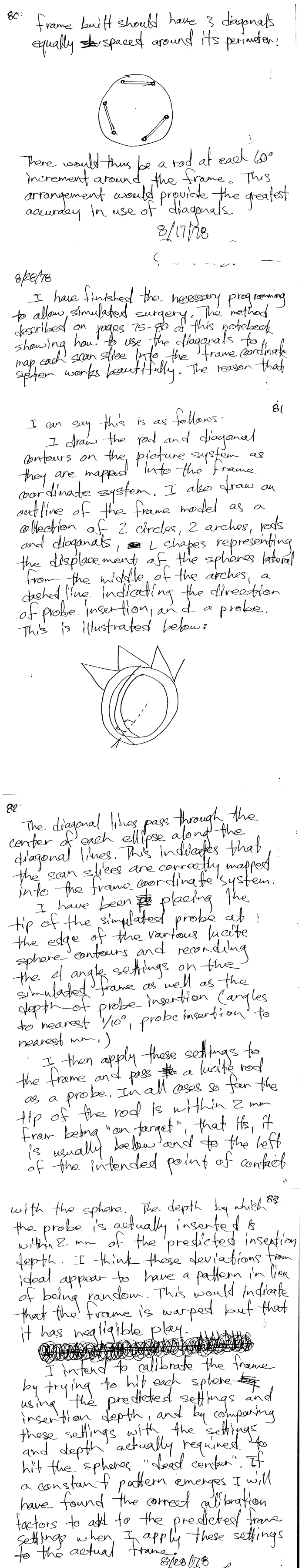
The rotation would be detected in the same manner as rotation about the z-axis.

Wednesday 5/31/78

7 Jun 1978

FIGURE 4: Appendix 2: 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 its, it is usually below and to the left of the intended point of contact

83

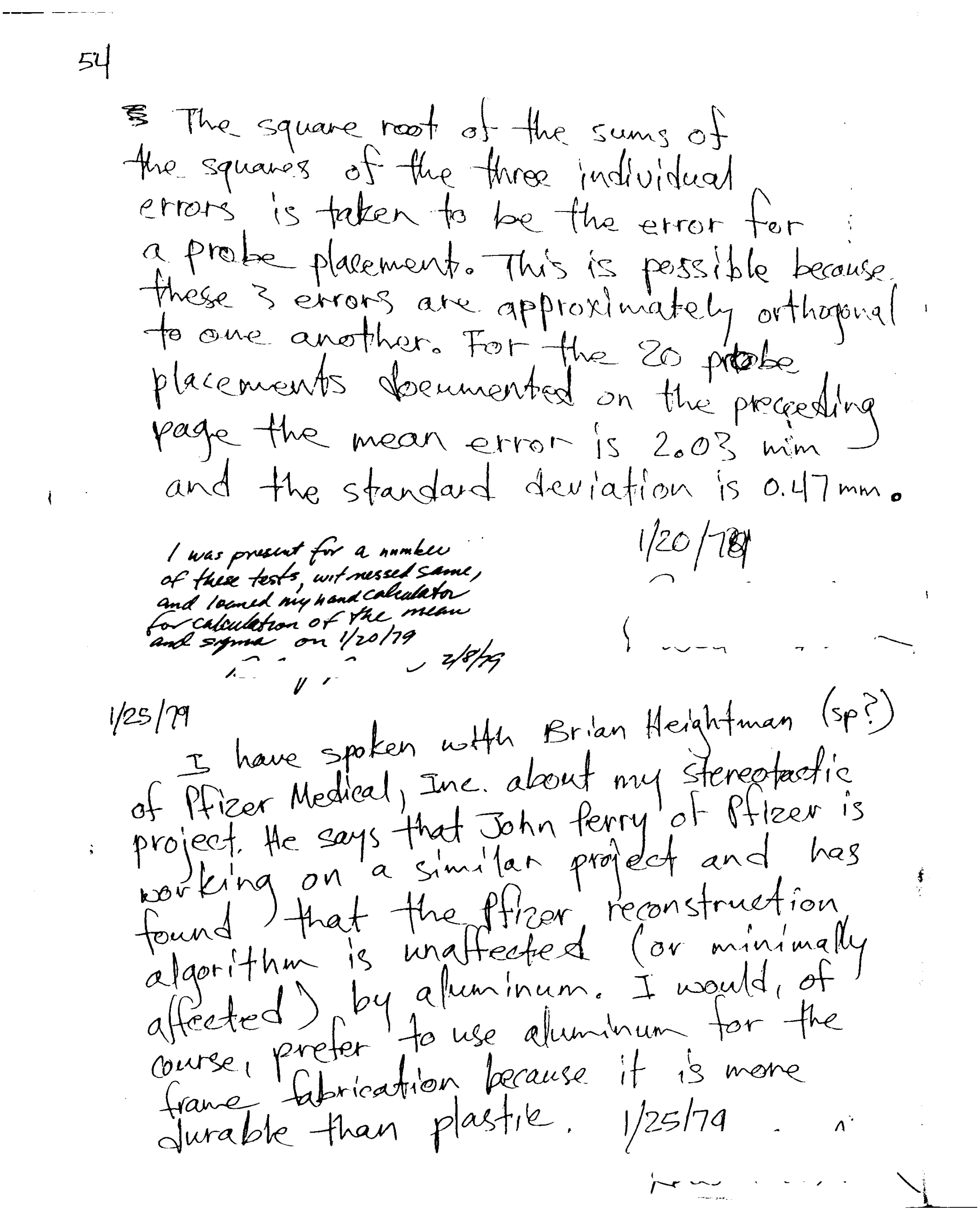
with the sphere. The depth by which the probe is actually inserted is within 2 mm of the predicted insertion depth. I think these deviations from ideal appear to have a pattern in lieu of being random. This would indicate that the frame is warped but that it has negligible play.

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 5: Appendix 3: 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 6: Appendix 4: Russell Brown Notebook 2, p. 54, January 25, 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

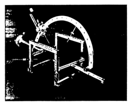
9052 Old Annapolis Road Columbia, Maryland 21045

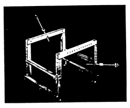
EXHIBIT A

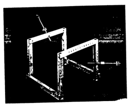
Explanation of Photographs

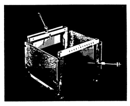
1. The standard stereotactic frame
2. The standard stereotactic frame with protractor
3. The standard stereotactic frame without protractor or protractor support bars
4. Stereotactic frame of figure 3 showing the placement of the fiducial plates.
5. Standard stereotactic frame mounted on head (Note the 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.

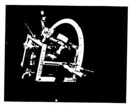
8. &
9. Are different views of the stereotactic frame ready for a scan with fiducial plates installed and the entire assembly mounted on the phantom's head.

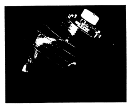


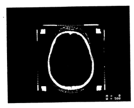


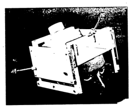












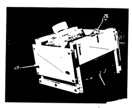
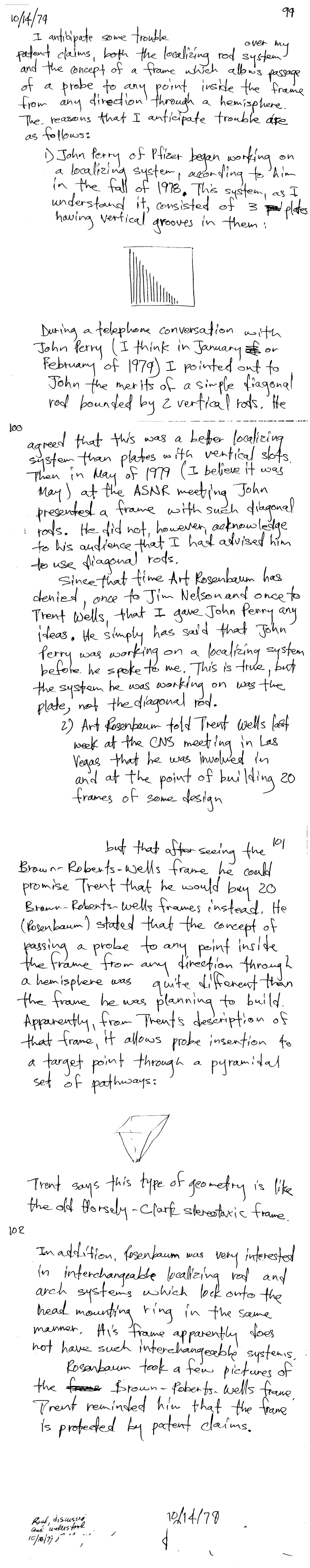


FIGURE 7: Appendix 5: Richard Matthews Letter, pp. 1-7,

January 26, 1979



10/14/79 99

I anticipate some trouble over my patent claims, both the localizing rod system and the concept of a frame which allows passage of a probe to any point inside the frame from any direction through a hemisphere. The reasons that I anticipate trouble are as follows:

1) John Perry of Pfizer began working on a localizing system, according to him in the fall of 1978. This system, as I understand it, consisted of 3 plates having vertical grooves in them:

During a telephone conversation with John Perry (I think in January or February of 1979) I pointed out to John the merits of a simple diagonal rod bounded by 2 vertical rods. He

100

agreed that this was a better localizing system than plates with vertical slots. Then in May of 1979 (I believe it was May) at the ASNR meeting John presented a frame with such diagonal rods. He did not, however, acknowledge to his audience that I had advised him to use diagonal rods.

Since that time Art Rosenbaum has denied, once to Jim Nelson and once to Trent Wells, that I gave John Perry any ideas. He simply has said that John Perry was working on a localizing system before he spoke to me. This is true, but the system he was working on was the plate, not the diagonal rod.

2) Art Rosenbaum told Trent Wells last week at the CNS meeting in Las Vegas that he was involved in and at the point of building 20 frames of some design

but that after seeing the 101

Brown-Roberts-Wells frame he could promise Trent that he would buy 20 Brown-Roberts-Wells frames instead. He (Rosenbaum) stated that the concept of passing a probe to any point inside the frame from any direction through a hemisphere was quite different than the frame he was planning to build. Apparently, from Trent's description of that frame, it allows probe insertion to a target point through a pyramidal set of pathways:

Trent says this type of geometry is like the old Horsely-Clark stereotaxic frame.

102

In addition, Rosenbaum was very interested in interchangeable localizing rod and arch systems which lock onto the head mounting ring in the same manner. His frame apparently does not have such interchangeable systems.

Rosenbaum took a few pictures of the ~~frame~~ Brown-Roberts-Wells frame. Trent reminded him that the frame is protected by patent claims.

Read, discussed and understood 10/18/79

10/14/79

FIGURE 8: Appendix 6: Russell Brown Notebook 3, pp. 99-102,

October 14, 1979

MAIL ROOM DEC 3 1985 PATENT & TRADEMARK OFFICE

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

RECEIVED
DEC 6 - 1985
BOARD OF APPEALS AND INTERFERENCES

Russell A. Brown,	)	
Junior Party,	)	Patent Interference
v.	)	No. 101,267
John H. Perry,	)	
Senior Party.	)	

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

Additional Information

Disclosures

Conflicts of interest: The authors have declared that no conflicts of interest exist.

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