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(54) **Title**: TOOL AND METHOD FOR ALIGNING A TISSUE PLANE FOR MICROTOMY

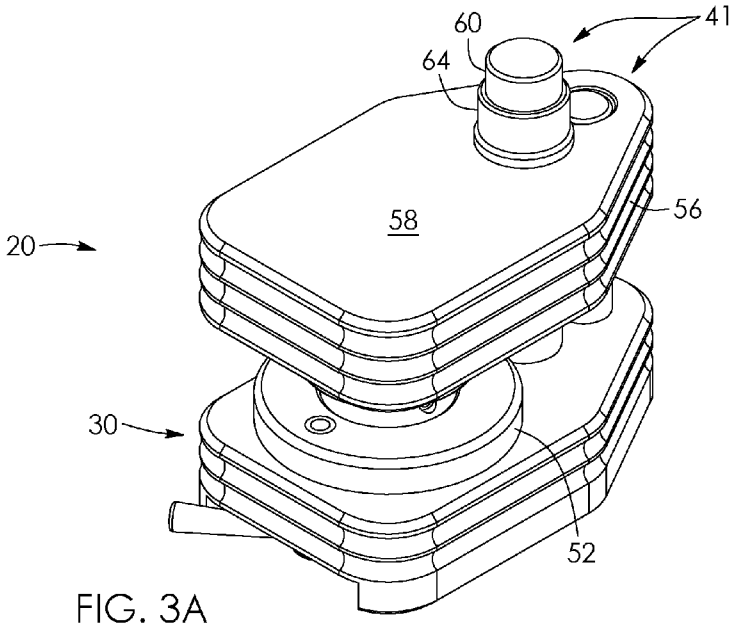


FIG. 3A

(57) **Abstract**: A tool and a method are provided, for applying a correction on a resection margin of a tissue block, in order to align the resection margin with the cutting plane of a microtome. The correction is determined using an embedding block having been cut by the microtome. The tool comprises a base, a chuck receiver, a positioning assembly comprising a flat surface and a bi-axial pivoting assembly operatively connected to one of the chuck receiver and the positioning assembly. The positioning assembly and the chuck receiver are movable one relative to the other for pressing the embedding block between said flat surface of the positioning assembly and the top surface of the chuck, for tilting the bi-axial pivoting assembly according to a compensating angle indicative of the correction to make.

TOOL AND METHOD FOR ALIGNING A TISSUE PLANE FOR MICROTOMY

FIELD OF THE INVENTION

The present invention relates to the field of microtomy, and more particularly, the present invention relates to a tool and a method for aligning a tissue plane for Mohs micrographic surgery.

BACKGROUND OF THE INVENTION

Mohs micrographic surgery is a surgical technique for removing tumorous cells involving a repeated series of surgical excisions followed by microscopic examination of the tissue to assess if any tumorous cells remain. Essentially, the examination of the tissue during the procedure informs the surgeon where to remove tissue next and the surgeon performing the procedure is generally also the pathologist reading the tissue specimen slides.

Mohs surgical procedure typically involves the following steps, represented by Figs 1A to 1G. In step 1A, narrow resection margins are made around a grossly identifiable tumor. In step 1B, notches are made in the tissue sample and in surrounding normal tissue for conserving orientation during the procedure. In step 1C, the resected tumor is prepared in such a way that the complete resection margin is presented in one plane. At this point, colored inks are used to identify the notches. In step 1D, a microscope slide is made from the prepared sample that shows the path of the surgeon's knife. In step 1E, the slide is interpreted under a microscope for the presence of tumorous cells. In step 1F, the areas having tumorous cells are mapped on a graphic representation of the surgical site. In step 1G, the surgeon follows the map and removes remaining tumorous areas, where needed. The steps are repeated until no tumorous cells remain.

The goal of Mohs surgery is to completely remove all tumor tissues with the minimal amount of tissue loss. By examining complete on face tissue margins, the surgeon can be confident that the tumor is completely excised. By removing the tissue in multiple, very thin layers, the point at which no tumor remains will become obvious with the least amount of tissue excised.

The Mohs surgeon, also acting as pathologist, relies on the microscope slide prepared

by a technician for diagnosis. However, the task of preparing an accurate representation of the resection margin has multiple pitfalls. More particularly, errors of flatness and errors of knife alignment are not resolved by known techniques presented hereinbelow.

In the Cryoembedder technique, also described in U.S. patent no. 7,059,139 issued to Marsing et al., a cryoembedder consists of a two-part jig that can accept the cryostat chuck on one part and a smooth disk on the second part. The tissue is frozen with the resection margin down on the smooth disk and the disk is placed on one of the jig faces. The cryostat chuck is placed in the other jig face and covered with embedding medium. When the embedding medium begins to freeze, the two jig faces are brought together and the sample to the chuck is frozen. Once frozen, the jig is separated and the smooth disk is broken free from the chuck-specimen-disk sandwich. The chuck is then ready for sectioning. Unfortunately, the Cryoembedder technique assumes that the object head is parallel to the knife holder, and due to the sliding fit clearance of the alignment pins of the jig, the faces may not always be parallel.

Also known as the Slide technique, the tissue is frozen flat against a glass microscope slide with the resection margin down against the slide. The technician is able to look under the slide to see if the surface of the tissue is making proper contact with the slide and corrections can be made before proceeding with the study. The slide is placed on the freeze bar for freezing. An embedding medium is poured around and over the tissue. A chuck is placed in the freezing bar and covered in embedding medium. As soon as the embedding medium begins to solidify on the slide, the tissue-slide block is flipped over to freeze on top of the chuck. Alternatively, the tissue covered in embedding medium is allowed to freeze completely. The slide is then removed from the cryostat and a warm hand is used under the glass slide to soften the tissue-embedding medium block. The tissue-embedding medium block is then freed from the glass. The tissue-embedding medium block is placed back in the cryostat and the chuck is placed in the freeze bar. The embedding medium is added on top of the chuck and as it freezes, the tissue-embedding medium block is placed on the chuck resection margin side up. However, one drawback with the Slide technique is that the tissue is frozen flat but not aligned with the knife.

In the Miami Special technique, a plier style (scissor, clamp) tool with wide jaws is used. One of the jaws has a hole or slot for accepting a chuck. Tissue is frozen flat using any

technique the technician prefers, such as in the Slide technique described above. The tissue-embedding medium block is freed from the slide and placed against the smooth jaw. A chuck with embedding medium is placed on the modified jaw and the two jaws are brought together by squeezing the handles together. The jaws are then submerged in liquid nitrogen to freeze the tissue-embedding medium block solid. The jaws are removed from the liquid nitrogen, opened and the chuck is removed for use. However, drawbacks of the Miami Special technique relate to the need for liquid nitrogen and the angle that the jaw closes at sets the plane of the resection margin in relation to the chuck. Thicker specimens are set at a greater angle than thinner specimens.

Many cryostat manufacturers include a heat extractor with their units in which a mobile heat sink device is used for flattening and speeding the freezing of specimens. In the Heat Extractor technique, the heat extractor is essentially a chrome-plated metal weight with a smooth flat underside that is kept in the cryostat in order to keep it cooled. In previous practices, a chuck with embedding medium was placed on the freeze bar. The tissue was placed on top of the solidifying embedding medium and then the heat extractor was place on top of the tissue to flatten and freeze it. In recent years, Mohs technicians have begun using the flat underside in the same manner as done in the Slide technique. However, the tissue quickly freezes to the cold metal surface. Once frozen, the tissue is covered with embedding medium and a chuck is prepared on the freeze bar with embedding medium. The two are brought together and the block quickly freezes. One drawback of the Heat Extractor technique is that it is hard to get the tissue to freeze at the correct angle to match the angle of the knife.

In the Precision Cryoembedding System technique, also described in US 2002/0162337 A1 originally assigned to Stephen Peters, there is a metal bar that has a series of shallow flat bottomed wells. The wells are cut with a tapered mill. All the surfaces are smoothly polished and, in conjunction with the sloped sides, the embedding medium is aided in breaking free. The tissue is frozen flat to the bottom of the well and is covered in embedding medium until the well is full. A chuck is placed upside down on top of the well, in order for the peripheral edge of the chuck to rest on the edges of the well, which keeps the face of the chuck parallel to the bottom of the well. Once frozen, the stem of the chuck is jarred and the tissue-embedding medium-chuck block is freed from the mold. The drawbacks associated with the Precision Cryoembedding System technique

are that not all chucks work with this system, as some chucks are stemless, and it is not possible to compensate for the knife angle as the tissue is parallel to the chuck face.

In the Plastic Molds technique, similar to that of the Precision Cryoembedding System but with thin plastic molds, the transparent molds freeze slower and allow the technician to look under the mold to see if the tissue is making proper contact in the center of the mold. A chuck can be frozen to the top of the mold or the tissue block can be popped out from the mold and mounted using any other technique known in the art. However, some drawbacks of the Plastic Molds technique are slow freezing; the molds are too small for larger specimens and difficult to compensate for knife angles.

Other techniques known in the art, such as the technique described in U.S. patent no. 5,776,298 issued to Franks, have drawback similar to the techniques described above.

Thus, known techniques for microtomy in the field of Mohs micrographic surgery lack the full set of attributes needed for minimizing tissue loss in sectioning when the tissue is aligned on a chuck, while minimizing errors of flatness and errors of knife alignment. There therefore exists a need in the art for a tissue aligning tool and method for preparing a tissue plane on a chuck for microtomy which alleviates at least some of the drawbacks of the prior art. The aligning tool and method may also be used for other surgical procedures, such as examination of a kidney tissue, or any other procedure requiring aligning a tissue plane with a reference plane, such as a cutting plane.

SUMMARY OF THE INVENTION

The object of the present invention is to provide a tool and a method whichsatisfies at least one of the above-mentioned needs and is thus an improvement over other related alignment systems and/or methods known in the prior art.

In accordance with the present invention, the above mentioned object is achieved, as will be easily understood, by a tool and a method such as the one briefly described herein and such as the one exemplified in the accompanying drawings.

According to an aspect of the invention, a tool for aligning a resection margin with the cutting plane of a microtome is provided. The tool comprises a base, a chuck receiver, a positioning assembly and a bi-axial pivoting assembly. The chuck receiver is typically mounted to the base and is for receiving a chuck. As well known in the art, a chuck has a

top surface for supporting embedding blocks. The bi-axial pivoting assembly operatively is connected to the chuck receiver or to the positioning assembly. The positioning assembly and the chuck receiver are movable one relative to the other for pressing the embedding block between a flat surface of the positioning assembly and the top surface of the chuck, so as to tilt the bi-axial pivoting assembly according to a compensating angle indicative of the correction to make. A locking mechanism allows locking the bi-axial pivoting assembly in the complementing position.

According to a possible embodiment of the tool, the bi-axial pivoting assembly is mounted to the base and comprises the chuck receiver.

According to a possible embodiment of the tool, the positioning assembly is lowerable toward the bi-axial pivoting assembly, for pressing the embedding block between the flat surface of the positioning assembly and the top surface of the chuck.

According to a possible embodiment of the tool, the bi-axial pivoting assembly is a ball-joint assembly.

According to a possible embodiment of the tool, the tool further comprises a chuck locking mechanism mounted on the chuck receiver, configured to lock the chuck in the chuck receiver. For example, the chuck receiver can include a threaded aperture and a locking pin, such that the threaded aperture receives the locking pin to lock the chuck in the chuck receiver. Of course, other locking mechanism can be considered, such as a high friction assembly between the bi-axial assembly and the base.

According to a possible embodiment of the tool, the positioning assembly can include a plate. The plate comprises a top surface and a lower surface, which includes the flat surface. The plate preferably has a tapered end, for providing increased clearance when removing the chuck from the chuck receiver.

According to a possible embodiment of the tool, the positioning assembly includes a guiding assembly mounted onto to the base, configured to cause the positioning assembly to move perpendicularly to the base. The guiding assembly can include at least one shaft mounted perpendicular onto to the base, the plate being provided with corresponding aperture(s) for receiving each of the least one shaft. The shaft(s) allows the positioning assembly to slide thereon. Preferably, the tool includes two shafts. The

shaft(s) and the plate are also preferably removably connected.

Preferably, the plate has its top surface opposite to the lower, flat surface. The plate can include at least one flange positioned coaxially with each aperture. The flange(s) extend outwardly from each surface, in order to maintain the flat surface perpendicular to the at least one shaft.

The tool can comprise the chuck. The chuck typically comprises a platform, and may include a stem extending therefrom. The platform has a sidewall which is preferably provided with a groove for positioning the chuck in a predetermined orientation in the chuck receiver or in the microtome.

According to another aspect of the present invention, a method is provided for aligning a resection margin of a tissue block with the cutting plane of a microtome in a cryostat. The method comprises the steps of:

a) providing an embedding block having opposed first face and second face, the second face resting on the top surface of a chuck;
b) placing the chuck in the microtome and cutting the first face of the embedding block, the cut first face of the embedding block forming thereafter an angle with the top surface of the chuck, said angle corresponding to a compensating angle between the top surface of the chuck and the cutting plane of the microtome;
c) determining an angle formed between the cut first face of the embedding block and the top surface of the chuck thereby corresponding to a misalignment angle; and
d) placing the chuck in a tool comprising a positioning assembly, the positioning assembly comprising a flat surface, the tool positioning the top surface of the chuck at an angle corresponding to the misalignment angle relative to the flat surface of the positioning assembly.

According to a preferred embodiment of the method, the step of determining the angle in step c) comprises the sub-steps of:

– placing the chuck with embedding block, cut in previous step, in a tool comprising bi-axial pivoting assembly;

- lowering a horizontal flat surface toward the bi-axial pivoting assembly until the horizontal flat surface presses on the cut first face of the embedding block, thereby tilting the bi-axial pivoting assembly in a complementing position, an angle formed between the horizontal flat surface of the positioning assembly and the top surface of the chuck thereby corresponding to a misalignment angle; and
- locking the bi-axial pivoting assembly in the complementing position and removing the embedding block from the tool.

Preferably, cutting the first or exposed face of the embedding block is made by cutting its entire surface. The embedding block used in step a) may solely comprises embedding medium or it may include the tissue sample. In the latter case, the embedding block corresponds to the tissue block.

The method may further comprises the steps of:

- placing a tissue sample having been previously frozen and flattened on the top surface of the chuck;
- embedding the tissue sample with embedding medium to form the tissue block having opposed first face and second face, the first face of the tissue block corresponding to the resection margin of the tissue sample, the second face resting on the top surface of the chuck,
- placing the chuck with the tissue block in the tool comprising the positioning assembly;
- moving the horizontal flat surface relative to the first face of the tissue block until the horizontal flat surface presses on the first face of the tissue block, thereby remodeling the tissue block such that the first face of the tissue block being parallel to the flat surface and forming a remodeling angle between the first face of the tissue block and the top surface of the chuck, said angle corresponding to the misalignment angle;
- allowing the embedding medium of the tissue block to freeze; and
- removing the chuck from the tool and placing the chuck in the microtome for cutting layers of the tissue block, the first face of the tissue block, remodelled in previous step, being therefore parallel to the cutting plane of the microtome, the

misalignment angle of the tissue block cancelling the compensating angle between the cutting plane and top surface of the chuck.

The objects, advantages and features of the present invention will become more apparent upon reading of the following non-restrictive description of preferred embodiments thereof, given for the purpose of exemplification only, with reference to the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1A to 1G schematically illustrates the general steps of a Mohs surgical procedure (PRIOR ART).

Figure 2A is a perspective view of a tool, in accordance with a possible embodiment of the present invention.

Figure 2B is another perspective view of Figure 2A, with an element of the tool removed.

Figure 2C is a side view of the tool of Figure 2A.

Figure 3A is a perspective view of a tool in accordance with another embodiment of the present invention.

Figure 3B is another perspective view of Figure 3A, with an element removed.

Figure 3C is a side view of the tool of Figure 3A.

Figure 4A is an exploded view of the tool shown in Figure 2A.

Figure 4B is an exploded view of the tool shown in Figure 3A.

Figures 5A to 5J schematically illustrate the general steps of a method for aligning a resection margin with the cutting plane of a microtome, according to a possible embodiment.

Figure 6A and 6B are block diagrams representing the different steps of the method, according to a possible embodiment.

DESCRIPTION OF PREFERRED EMBODIMENTS OF THE INVENTION

It is to be understood that certain descriptions of the present invention have been simplified to illustrate only those elements and limitations that are relevant to a clear understanding of the present invention, while eliminating, for purposes of clarity, other elements. Those of ordinary skill in the art, upon considering the present description of the invention, will recognize that other elements and/or limitations may be desirable in order to implement the present invention. However, because such other elements and/or limitations may be readily ascertained by one of ordinary skill upon considering the present description of the invention, and are not necessary for a complete understanding of the present invention, a discussion of such elements and limitations is not provided herein. As such, it is to be understood that the description set forth herein is merely exemplary to the present invention and is not intended to limit the scope of protection.

It is worth mentioning that throughout the following description, when the article “a” is used to introduce an element, it does not have the meaning of “only one” it rather means of “one or more”.

As used herein, the expression “resection” is intended to refer to surgical removal of a portion of any part of the body. There can be a second resection done in the lab called a pathological resection margin and in that case the initial cut becomes the surgical resection margin.

As used herein, the expression “resection margin” is the margin of apparently non-tumerous tissue around the cancerous portion of a tissue sample that has been surgically removed.

As used herein, the term “tissue” is intended to refer to any group of biological cells that perform a similar function.

As used herein, the term “microtomy” is intended to refer to the science or practice of preparing extremely thin slices of tissue, etc., cut by a microtome, for study under the microscope.

As used herein, the term “microtome” is intended to refer to a tool used to cut extremely thin slices of material, known as sections. Microtomes are used in microscopy, allowing for the preparation of samples for observation under transmitted light or electron radiation. Microtomes use steel, glass, or diamond blades depending upon the specimen

being sliced and the desired thickness of the sections being cut. Also, the specimen may be raised and lowered across a stationary blade. Alternatively, some models move a blade across a stationary sample and others use a vibrating blade to cut through harder samples.

Moreover, although the preferred embodiment of the present invention as illustrated in the accompanying drawings comprises components such as a bi-axial pivoting assembly, a plate, a base, etc., and although the preferred embodiment of the tool to align the resection margin with the cutting plane of a microtome and corresponding parts thereof consists of certain geometrical configurations as explained and illustrated herein, not all of these components and geometries are essential to the invention and thus should not be taken in their restrictive sense, i.e. should not be taken as to limit the scope of the present invention. It is to be understood, as also apparent to a person skilled in the art, that other suitable components and cooperations thereinbetween, as well as other suitable geometrical configurations may be used for the tool to align the resection margin with the cutting plane of a microtome according to the present invention, as will be briefly explained herein and as can be easily inferred herefrom, by a person skilled in the art, without departing from the scope of the invention.

In the following description, similar features in the drawings have been given similar reference numerals. The embodiments, geometrical configurations, materials mentioned and/or dimensions shown in the figures or described in the present description are preferred embodiments only, given for exemplification purposes only.

Furthermore, the order of the steps of the method described herein should not be taken as to limit the scope of the invention, as the sequence of the steps may vary in a number of ways, without affecting the scope or working of the invention, as can also be understood.

Devices known in the art are unable to keep the tissue plane of the sample parallel to path of the knife. They focus solely on keeping the tissue plane parallel to the face of the chuck, falsely assuming that the path of the blade is square with the chuck. The knife that cuts this face can be off by as much as 0.158° degrees (this was measured as 0.0185" displacement over a 6.6929" run), which results in a loss of 69μ (Microns) of tissue on a 25mm wide tissue sample.

The coupling device on the object head of other devices known in the art pushes the chuck a much as 0.010″ out of alignment over a 1.578″ diameter chuck. This results in a 0.363° error and, to relate this to the previous example, equals 158μ of tissue loss for a 25mm wide sample.

The ball detent that technicians rely on in the art to zero the object head can be off by as much 0.045″ over a 1.950″ face, and this equals 1.322° and a further 577μ of tissue loss for a 25mm sample. The locking arm for the XY axial adjustments on the object head can push the object head face out another 30 to 50μ more.

Some of the tools known in the art use a sliding fit on their jigs to bring two faces together in a parallel plane but the tolerances of this 0.010'' fit causes a 0.572º error or 250μ for a 25mm sample.

If we were to compound these errors, a total of 854μ is obtained or at the very least with some errors cancelling others 300μ is obtained without considering the help or hindrance of the other tool.

A micron is a very small unit so these miss alignments might at first glance seem trivial. However, the tissue sections cut on the microtome are generally 5-7μ thick and an average cell is 10-15 μ in diameter. It should be noted that a layer of 3 normal cells can make the difference between a false negative and a false positive for a broad group of diseases involving unregulated cell growth, such as cancer.

Broadly described, the tool for aligning the resection margin with the cutting plane of a microtome according to the present invention, as exemplified in the accompanying drawings, is a tool for applying a correction on a tissue block in order to align the resection margin of the tissue block with the cutting plane of a microtome. The correction is typically determined using an embedding block having been cut by the microtome, such that the actual cutting plane of the microtome is “transferred” to the cut embedding block.

For the sake of clarity, certain reference numerals have been omitted from the figures when they have already been identified in a preceding figure.

Referring to Figure 5A, a chuck 36 with an embedding block (28, 82) is shown. An embedding block typically consists of embedding medium which includes the tissue sample, with the resection margin of the tissue sample facing upwardly. In some cases, the embedding block may not include the tissue sample, and solely consists of frozen embedding medium, as will be explained in more detail below. Typically, when the embedding block comprises the tissue sample, it is referred to as a "tissue block".

The chuck 36 has a top surface 38 for supporting the block (28, 82). While the chuck shown in Figure 5A is provided with a stem, other configurations of chucks are possible, as is well known in the art. The embedding block (28 or 32) has a first face 74 facing upwardly when placed on the chuck, and a second, opposite face 76 resting on the chuck. The first face 74 can also be referred to as the "exposed" or "resection" face of the block. When the embedding block includes a tissue sample, the first face 74 includes the resection margin of the tissue sample.

Referring to Figure 5B, a schematic drawing of the blade 90 of a microtome and of the chuck 36 placed in the microtome is shown. As indicated by the arrow, the chuck can move back and forth relative to the blade 90 of the microtome, so as to slice thin layers of the tissue sample from the embedding block, similar to a meat slicer.

The cutting plane 26 is the actual cutting plane of the blade 90 in a microtome, and the theoretical cutting plane 260 is the ideal cutting plane which should be parallel to the first face 74 of the tissue sample, such that when the microtome slices layers of the tissue sample, the entire surface of the resection margin 24 of the tissue sample is cut.

As explained above, in theory, the cutting plane 26 of the microtome should be parallel to the top surface of the chuck 38, and the exposed face (or resection margin) of the tissue sample should also be parallel to the top surface of the chuck 38. The tissue sample is embedded in embedding medium, and, according to common practice, technicians will aim to freeze the embedding block 28 such that the top or exposed face of the block 74 is parallel to the top surface of the chuck 38.

However, in reality, the cutting plane 26 of microtome and the top surface of the chuck 38 are not parallel, and there is an angle between the two planes (*i.e.* cutting plane of microtome 26 and top surface of chuck 38 when placed in microtome). Thus, if the first surface 74 of the embedding block 28 is frozen such as to be as parallel as possible with

the top surface of the chuck 38, there will be an error or misalignment angle θ between the cutting plane of the tool 26, and the exposed surface 74 of the embedding block 28.

The tool 20 and method of the present invention aims to align the first or resection face 24,74 of the embedding block 28 with the actual cutting plane of the microtome blade. One possible way of achieving this alignment is by remodeling or reshaping the embedding block 28 such that the first/resection face 74 of the embedding block 28 is coplanar with the cutting plane of the microtome.

Method for aligning the resection margin of a tissue block with the cutting plane of a microtome in a cryostat

Referring now to Figures 5C to 5J, a method for aligning the resection margin of a tissue block 22 with the cutting plane 26 of a microtome in a cryostat will be described, according to a possible implementation.

The method may be divided into two main stages: 1) determining the misalignment angle, as illustrated in Figure 6A and 2) remodelling the tissue block 22 to compensate for the misalignment angle, as illustrated in Figure 6B.

Referring to Figure 5C, in a first stage of the method, an embedding block 28 is provided 600 and placed on the top surface of the chuck 38. In this step, the embedding block 28 does not necessarily comprise the tissue sample, since this step initially consists in determining the correction angle to apply for future tissue sample to be processed. The embedding block 28 has opposed first face 74 and second face 76. The second face 76 rests on the top surface of the chuck 38. The embedding block 28 can be made of any suitable material such as an embedding medium, a tissue block 22, polyvinyl alcohol and the like, as apparent to a person skilled in the art. The embedding block 28 may be used as a test block in order to capture the misalignment angle.

Still referring to Figure 5C, the first face 74 of the embedding block 28 is preferably cut 602 across the entire surface of the first face 74 to reduce reading errors of the misalignment angle. The cut first face 74 of the embedding block 28 forms thereafter an angle with the top surface of the chuck 38, as illustrated in Figure 5C, said angle corresponding to a compensating angle between the top surface 38 of the chuck 36 and the cutting plane 26 of the microtome.

The next step of the method is to determine 604 and reuse the misalignment angle. There are a number of ways to use to determine the misalignment angle. For example, by using a 3D image scanner or by using a tool comprising a bi-axial pivoting assembly 32 as the one described below and illustrated in Figure 5D.

Referring to Figure 5D, the chuck 36 is placed in the tool 20,606, comprising the bi-axial pivoting assembly 32. The bi-axial pivoting assembly 32 is mounted on to the base 30 and is free to rotate along the coplanar axis of the base 30. The tool 20 also comprises a positioning assembly 40 which includes a plate 56 having a horizontal flat surface 42 that can be moved vertically as shown in Figure 5D.

Referring to Figure 5E, the plate is lowered until the horizontal flat surface 42 presses on the cut first face 74 of the embedding block 28, thereby tilting the bi-axial pivoting assembly 32 in a complementing position. At this point, the angle θ formed between the top surface 38 of the chuck 36 and the cut first face 74 corresponds to the misalignment angle defined in Figure 5C. Once in this complementing position, the bi-axial pivoting assembly 32 can be locked and the chuck is removed, as illustrated in Figure 5F.

Referring to Figure 5G, in a second stage of the method, a tissue block is provided 608 and placed on the top surface of the chuck 38. The tissue sample has a resection margin 24 corresponding to the lowermost portion of the sample cut by the surgeon. An embedding medium (23) is applied 610 on the tissue sample to form a tissue block 22. The tissue block 22 has an exposed/outer face, and a second, opposite face. The second face rests on the top of face of the chuck 36.

Referring to Figure 5H, the chuck 36 is placed 612 in the tool 20 where the bi-axial pivoting assembly 32 was locked in the complementing position. At this stage, the plate of the positioning assembly is lowered until the horizontal flat surface 42 presses on the resection margin of the tissue block 22, thereby remodelling 614 the tissue block such that the resection margin 24 of the tissue block 22 is coplanar with the horizontal flat surface 42, as illustrated in Figure 5I. The exposed face of the tissue block 22 can be remodelled or reshaped because the emdedding medium is not completely frozen at this stage, and can thus be slightly remodelled by the flat surface of the positioning assembly, can in this case is comprised in the plate 56.

Referring to Figure 5I, the remodelled tissue block 22 now has its expose face,

corresponding to the resection margin 24 of the tissue sample, forming an angle θ with the top surface 38 of the chuck 36, where this angle corresponds to the misalignment angle. At this stage, the tissue block is allowed to freeze in the cryostat.

Referring to Figure 5J, once the tissue block is frozen 616, the chuck 36 can be placed in the microtome 61820 to layer the tissue sample so as to start the examination of the tissue sample. At this point, the resection margin 24 of the block 22 is parallel with the actual cutting plane of the microtome blade eliminating or at least greatly reducing the error or the misalignment angle θ between the cutting plane of the tool 20, and the resection margin 24 of the tissue block 22.

Tool for aligning the resection margin of a tissue block with the cutting plane of a microtome in a cryostat

Broadly described and referring to Figures 2A to 4B, there is shown the tool 20 for applying a correction on the resection margin 24 of a tissue block 22 in order to align the resection margin 24 with the cutting plane 26 of a microtome.

Referring to Figures 2A and 4A, the illustrated tool 20 comprises a base 30, a positioning assembly 40 and a bi-axial pivoting assembly 32.

The positioning assembly 40 includes a plate 56 that has a flat surface 42, and a guiding assembly 41. The flat surface 42 is used to press on a surface of a tissue block 22 or embedding block 28 to create a reference surface for angle measurements. The guiding assembly 41 is used to guide the relative movement between the flat surface 42 and the base 30. According to an embodiment, the guiding assembly may is mounted on the base 30 and comprises at least one shaft 60 and corresponding apertures 62 as illustrated in Figure 4A. The guiding assembly may optionally comprise a rail system, a controlled robotic arm, or the like, as apparent to a person skilled in the art. The guiding assembly may also be mounted on a support other than the base 30 in order to control the orientation and position of the positioning assembly 40 and to move the positioning assembly 40 and/or the chuck receiver 34 relative to each other. Referring to Figure 4A, the guiding mean comprises at least one shaft 60 mounted perpendicular onto to the base 30. The plate 56 comprises a corresponding aperture 62 for receiving each of the least one shaft 60. In this configuration, the guiding assembly allows the plate 56 to slide thereon to reach the tissue block 22 or the embedding block 28. In this configuration, the

weight of the plate 56 allows the flat surface 42 to press on the tissue block 22 or the embedding block 28 in order to align the resection margin 24 or the first surface of the embedding block according to the compensating angle. Optionally, the plate 56 includes at least one flange 64 positioned coaxially with each aperture 62 and extending outwardly from each surface of the plate 56 in order to maintain the flat surface 42 perpendicular to the at least one shaft 60, as shown in Figure 3A. The at least one shaft 60 and the plate 56 may also be removably connected. Optionally, the plate 56 may have a tapered end, as illustrated in Figure 2A, to provide increased clearance when lifting the plate 56 and placing or removing the chuck 36. In this preferred embodiment, two shafts are mounted to the base 30.

The tool (20) also comprises a chuck receiver 34 that is operatively mounted to the base 30 for receiving a chuck 36. Referring to Figure 4A, the chuck receiver comprises a threaded aperture and a locking pin 50 and is forming part of the bi-axial pivoting assembly. The chuck receiver may have different configurations such as a clamp, a press fitting mechanism and the like. The chuck receiver may also be mounted on the base 30 directly or being held by a device such as an arm and a clamp to receive the chuck 36. The chuck receiver may be mounted on the base 30 or on another support, as apparent to a person skilled in the art. In the configuration illustrated in Figure 4A, a protrusion 52 is added to house the chuck receiver 34 in the bi-axial pivoting assembly. To facilitate the movement of the locking pin 50 around the bi-axial pivoting assembly 32, the protrusion 52 around the bi-axial pivoting assembly 32 may have a recess 54 to allow further movement of the locking pin 50.

Referring to Figure 4B, there is shown a bi-axial pivoting assembly 32. The bi-axial pivoting assembly 32 is operatively connected to one of the chuck receiver 34 or the positioning assembly 40. The bi-axial pivoting assembly 32 may include a rotatable joint or any other joint assemblies, such as a ball-joint assembly. It may also include controllable servo-motors or any other controllable devices capable of orienting the positioning assembly 40 in a complementary position according to a given angle. Optionally, a locking mechanism 44 can be used to lock the bi-axial pivoting assembly 32 in a complementing position. A high friction connection between the bi-axial pivoting assembly and the base could also serve as a locking mechanism.

In the first scenario, where the bi-axial pivoting assembly can be mounted between the

base 30 and the chuck receiver 34 as illustrated in Figures 2B and 5D. In use, the chuck can be oriented such that the upper face of the tissue block/embedding block (24, 74) is coplanar with the flat surface 42 of the positioning assembly 40 and therefore capturing an angle between the upper surface (24, 74) and the flat surface 42 or tilting the bi-axial pivoting assembly 40 according to a compensating angle indicative of the correction to make.

In the second scenario, the bi-axial pivoting assembly can be operatively mounted on the positioning assembly 40. In this case, the chuck receiver can be mounted on the base 30 such as the orientation of the chuck when placed in the chuck receiver is fixed and can be used as a reference plane. In use, the bi-axial pivoting assembly be oriented such as the flat surface 42 of the positioning assembly 40 is coplanar with the upper face of the tissue block/embedding block (24, 74) in order to capture the angle between the upper surface (24, 74) and the flat surface 42 or tilting the bi-axial pivoting assembly 40 according to a compensating angle indicative of the correction to make.

The tool 20 may also include the chuck 36 wherein said chuck 36 has a platform 66 and a stem 68 extending therefrom, and wherein the platform 66 has a sidewall 70 that is provided with a groove 72. The groove 72 can be used for positioning the chuck 36 in a predetermined orientation. Using the groove 72 as a marker, the chuck 36 can be placed in the chuck receiver 34 with the same orientation in the steps of determining the misalignment angle formed by the cutting plane 26 and of remodeling the tissue block 22 for compensating the misalignment angle, as described below.

Numerous other modifications could be made to the above-described alignment method without departing from the scope of the present invention. The above-described embodiments are considered in all respect only as illustrative and not restrictive, and the present application is intended to cover any adaptations or variations thereof, as apparent to a person skilled in the art.

The above-described embodiments are considered in all respect only as illustrative and not restrictive, and the present application is intended to cover any adaptations or variations thereof, as apparent to a person skilled in the art. Of course, numerous other modifications could be made to the above-described embodiments without departing from the scope of the invention, as apparent to a person skilled in the art.

Claims

1. A tool for applying a correction on a resection margin of a tissue block, in order to align the resection margin with the cutting plane of a microtome, the correction being determined using an embedding block having been cut by the microtome, the tool comprising:
   - a base;
   - a chuck receiver operatively mounted to the base for receiving a chuck having a top surface for supporting the embedding block;
   - a positioning assembly comprising a flat surface;
   - a bi-axial pivoting assembly operatively connected to one of the chuck receiver and the positioning assembly, the positioning assembly and the chuck receiver being movable one relative to the other for pressing the embedding block between said flat surface of the positioning assembly and said top surface of the chuck, for tilting the bi-axial pivoting assembly according to a compensating angle indicative of the correction to make; and
   - a locking mechanism to lock the bi-axial pivoting assembly in a complementing position.

2. The tool according to claim 1, wherein the bi-axial pivoting assembly is mounted to the base and comprises the chuck receiver.

3. The tool according to claim 1 or 2, wherein the positioning assembly is lowerable toward the bi-axial pivoting assembly, for pressing the embedding block between the flat surface of the positioning assembly and the top surface of the chuck.

4. The tool according to anyone of claims 1 to 3, wherein the bi-axial pivoting assembly is a ball-joint assembly.

5. The tool according to anyone of claims 1 to 4, wherein the tool further comprises a chuck locking mechanism mounted on the chuck receiver, configured to lock the chuck in the chuck receiver.

6. The tool according to anyone of claims 1 to 5, wherein the chuck receiver 34 comprises a threaded aperture and a locking pin, the threaded aperture receiving the locking pin to lock the chuck in the chuck receiver.

7. The tool according to claim 1 to 6, wherein the positioning assembly comprises a plate, the plate comprising a top surface and the flat surface, wherein the plate has a tapered end providing increased clearance when removing the chuck from the chuck receiver.

8. The tool according to anyone of claims 1 to 7, wherein the positioning assembly comprises a guiding assembly mounted onto to the base, configured to cause the positioning assembly to move perpendicularly to the base.

9. The tool according to claim 8, wherein the guiding assembly comprises at least one shaft mounted perpendicular onto to the base and the plate comprising a corresponding aperture for receiving each of the least one shaft, the at least one shaft allowing the positioning assembly to slide thereon.

10. The tool according to claim 9, wherein the least one shaft and the plate are removably connected.

11. The tool according to claim 9 or 10, wherein the plate has the top surface opposite to the flat surface, said plate comprising at least one flange positioned coaxially with each aperture extending outwardly from each surface of the positioning assembly in order to maintain the flat surface perpendicular to the at least one shaft.

12. The tool according to anyone of claims 1 to 12, further comprising the chuck, the chuck comprising a platform and a stem extending therefrom and wherein the platform has a sidewall provided with a groove for positioning the chuck in a predetermined orientation.

13. A method for aligning a resection margin of a tissue block with the cutting plane of a microtome in a cryostat, comprising the steps of:

a) providing an embedding block having opposed first face and second face, the second face resting on the top surface of a chuck;
b) placing the chuck in the microtome and cutting the first face of the embedding block, the cut first face of the embedding block forming thereafter an angle with the top surface of the chuck, said angle corresponding to a compensating angle between the top surface of the chuck and the cutting plane of the microtome;

c) determining an angle formed between the cut first face of the embedding block and the top surface of the chuck thereby corresponding to a misalignment angle; and

d) placing the chuck in a tool comprising a positioning assembly, the positioning assembly comprising a flat surface, the tool positioning the top surface of the chuck at an angle corresponding to the misalignment angle relative to the flat surface of the positioning assembly.

14. The method according to claim 15, wherein step c) comprises the sub-steps of :

i) placing the chuck with embedding block cut in step b) in a tool comprising a bi-axial pivoting assembly;

ii) lowering a horizontal flat surface toward the bi-axial pivoting assembly until the horizontal flat surface presses on the cut first face of the embedding block, thereby tilting the bi-axial pivoting assembly in a complementing position, an angle formed between the horizontal flat surface of the positioning assembly and the top surface of the chuck thereby corresponding to a misalignment angle; and

iii) locking the bi-axial pivoting assembly in the complementing position and removing the embedding block from the tool.

15. The method according to claim 15 or 16, wherein in step b), cutting the first face of the embedding block is made by cutting an entire surface of the first face.

16. The method according to anyone of claims 15 to 17, wherin in step a), the embedding block solely comprises embedding medium.

17. The method according to anyone of claims 15 to 18, further comprising the steps of:

e) placing a tissue sample previously frozen and flattened on the top surface of the chuck;

f) embedding the tissue sample with embedding medium to form the tissue block having opposed first face and second face, the first face of the tissue block corresponding to the resection margin of the tissue sample, the second face resting on the top surface of the chuck,

g) placing the chuck with the tissue block in the tool comprising the positioning assembly;

h) moving the horizontal flat surface relative to the first face of the tissue block until the horizontal flat surface presses on the first face of the tissue block, thereby remodeling the tissue block such that the first face of the tissue block being parallel to the flat surface and forming a remodeling angle between the first face of the tissue block and the top surface of the chuck, said angle corresponding to the misalignment angle;

i) allowing the embedding medium of the tissue block to freeze; and

j) removing the chuck from the tool and placing the chuck in the microtome for cutting layers of the tissue block, the first face of the tissue block remodelled in step h) being therefore parallel to the cutting plane of the microtome, the misalignment angle of the tissue block cancelling the compensating angle between the cutting plane and top surface of the chuck.

18. The method according to claim 15, wherein in step a), the embedding block corresponds to the tissue block.

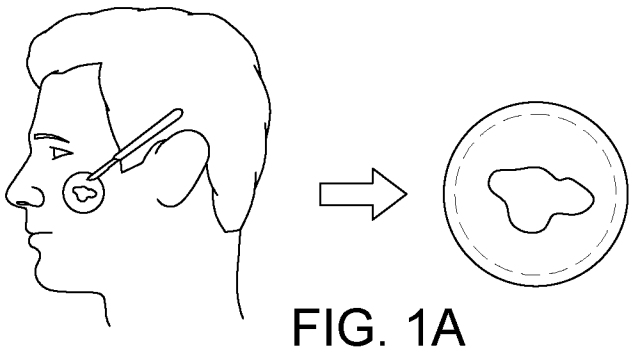


FIG. 1A
(PRIOR ART)

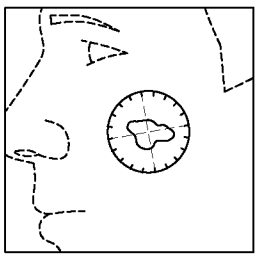


FIG. 1B
(PRIOR ART)

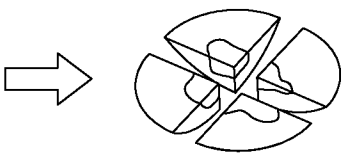


FIG. 1C
(PRIOR ART)

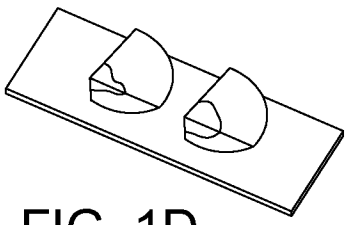


FIG. 1D
(PRIOR ART)

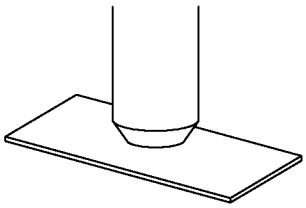


FIG. 1E
(PRIOR ART)

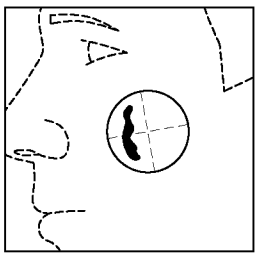


FIG. 1F
(PRIOR ART)

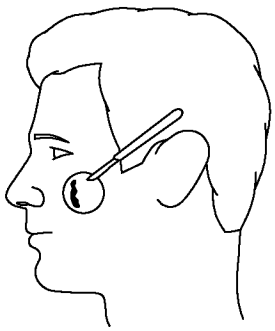


FIG. 1G
(PRIOR ART)

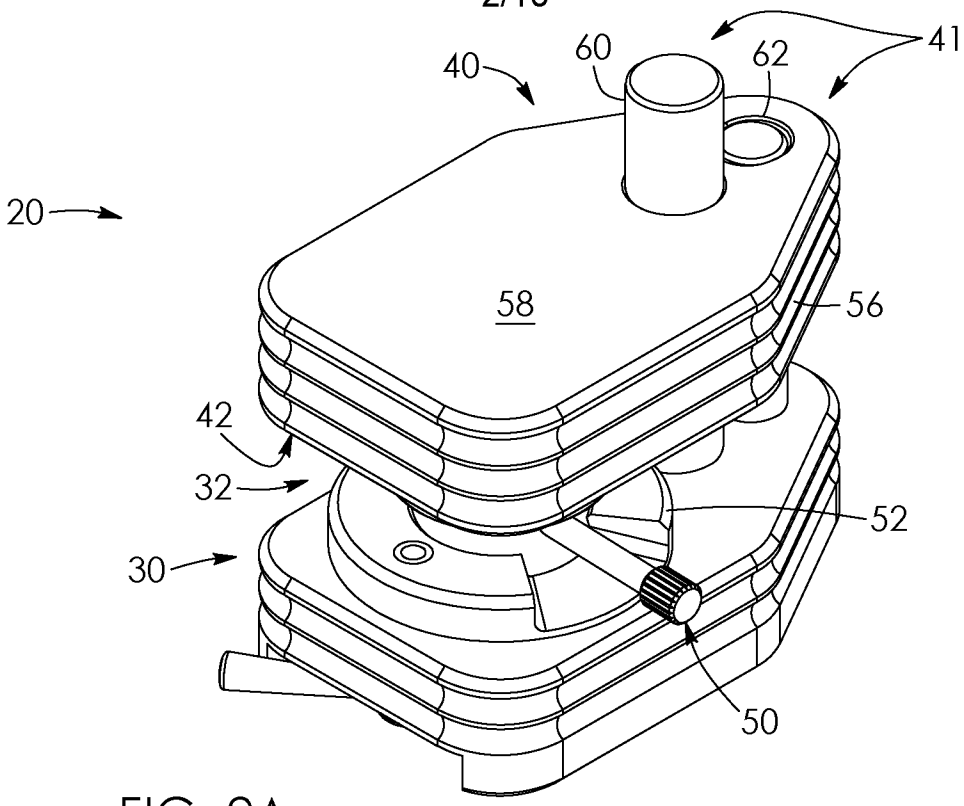


FIG. 2A

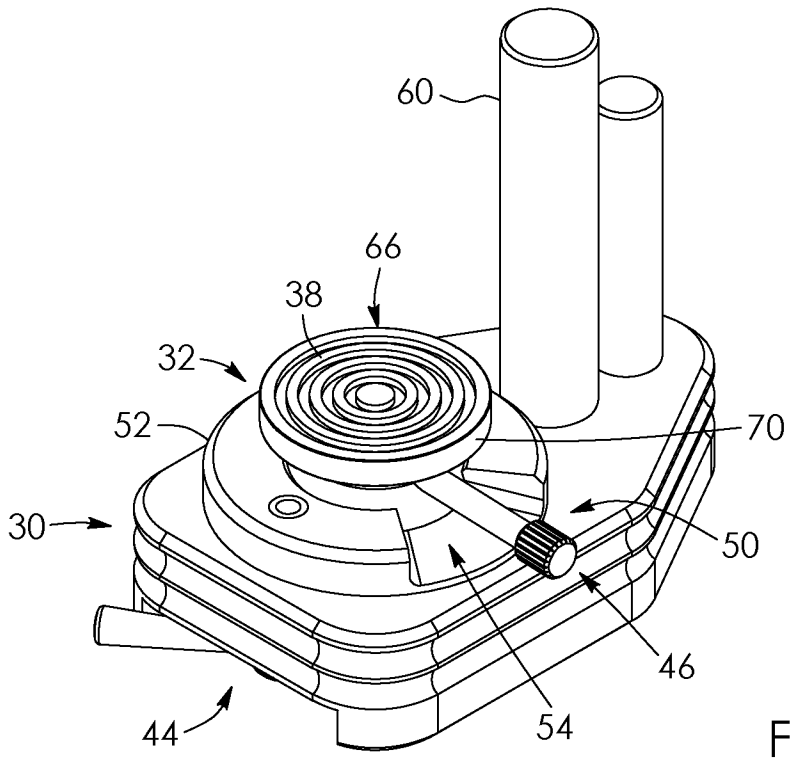


FIG. 2B

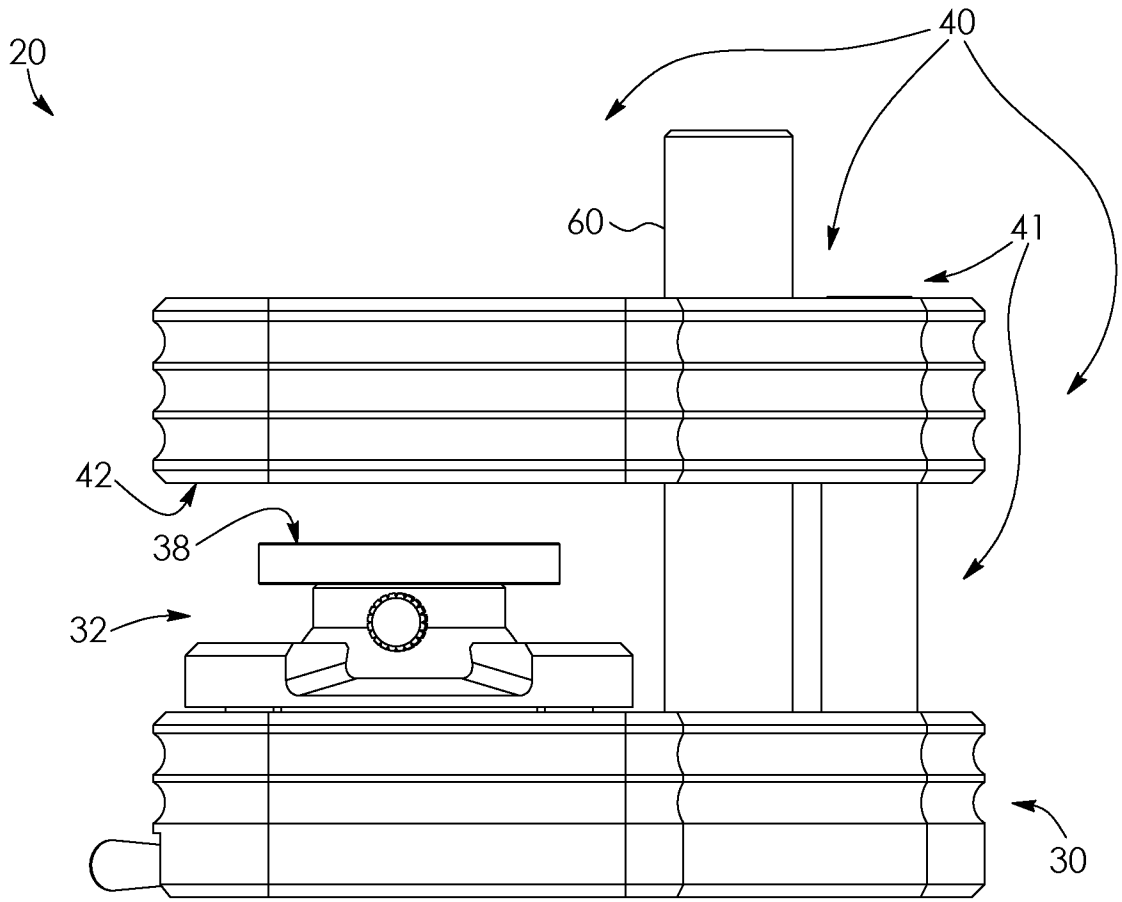


FIG. 2C

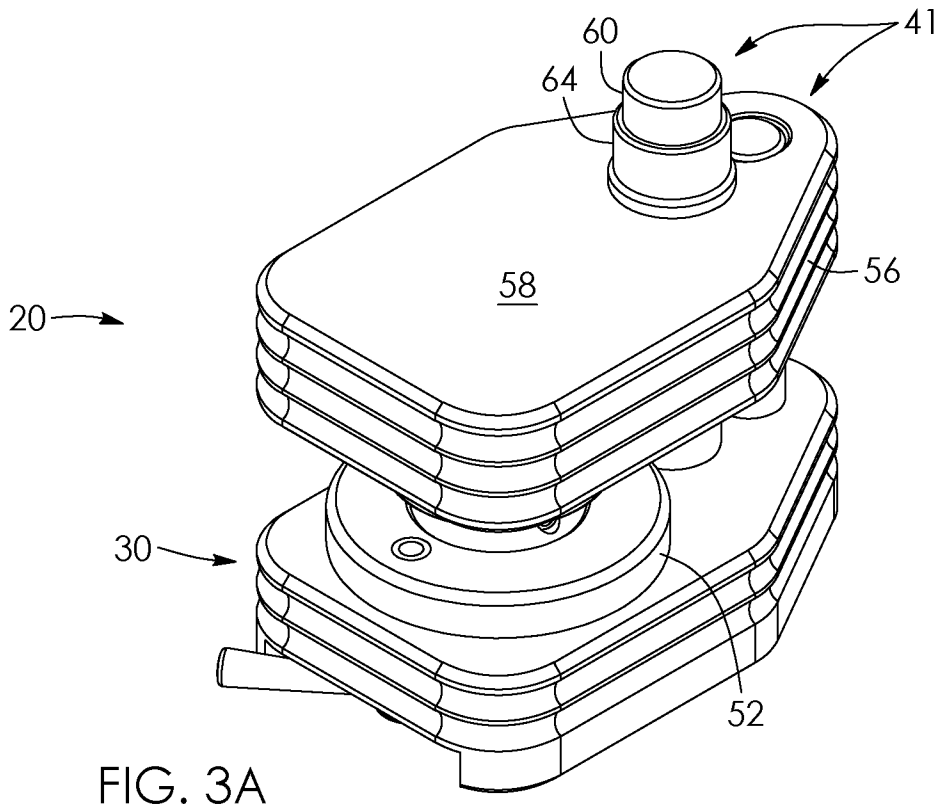


FIG. 3A

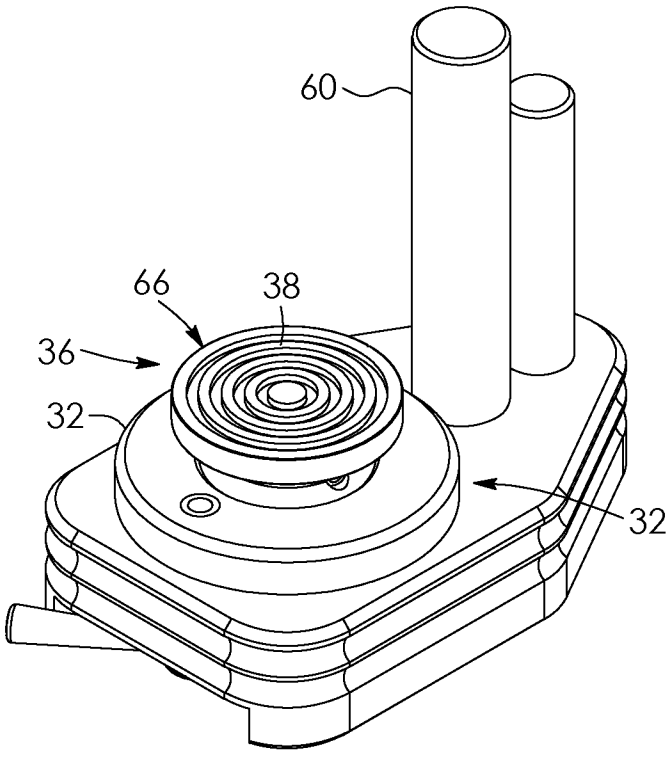


FIG. 3B

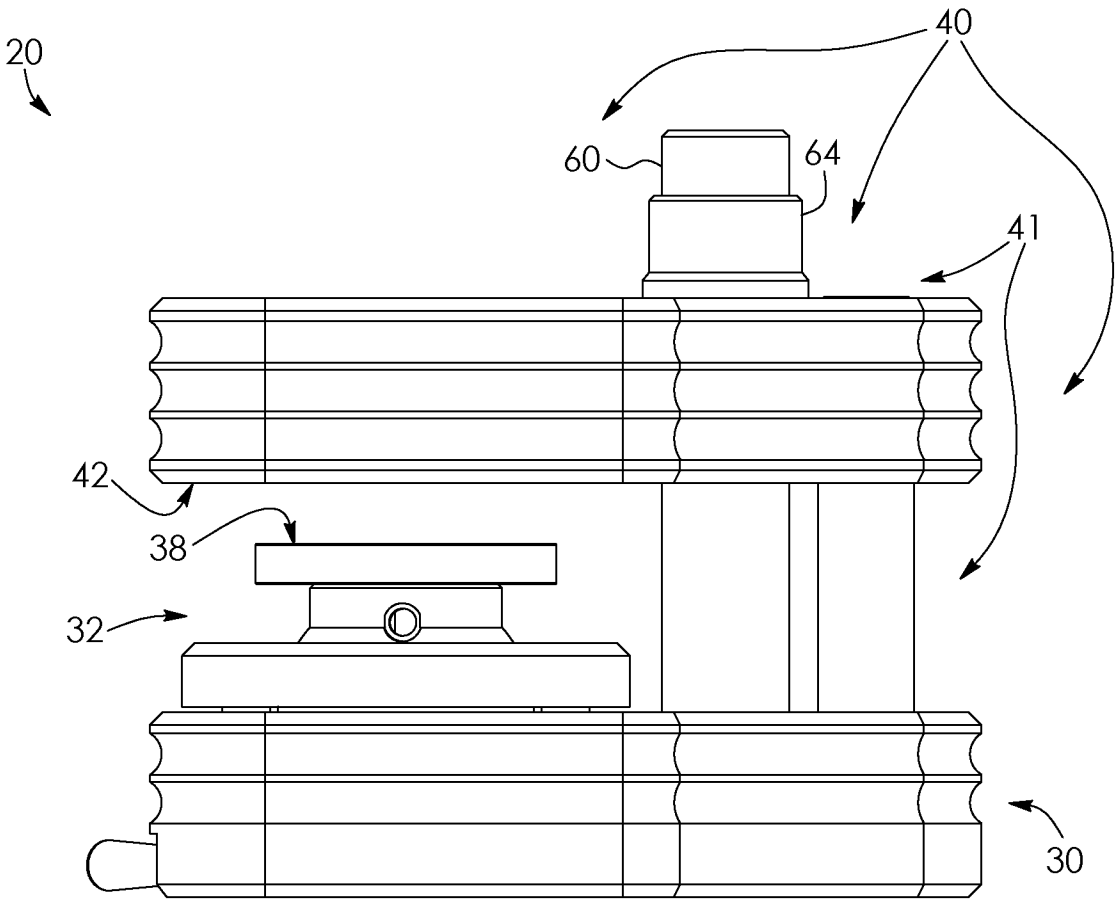


FIG. 3C

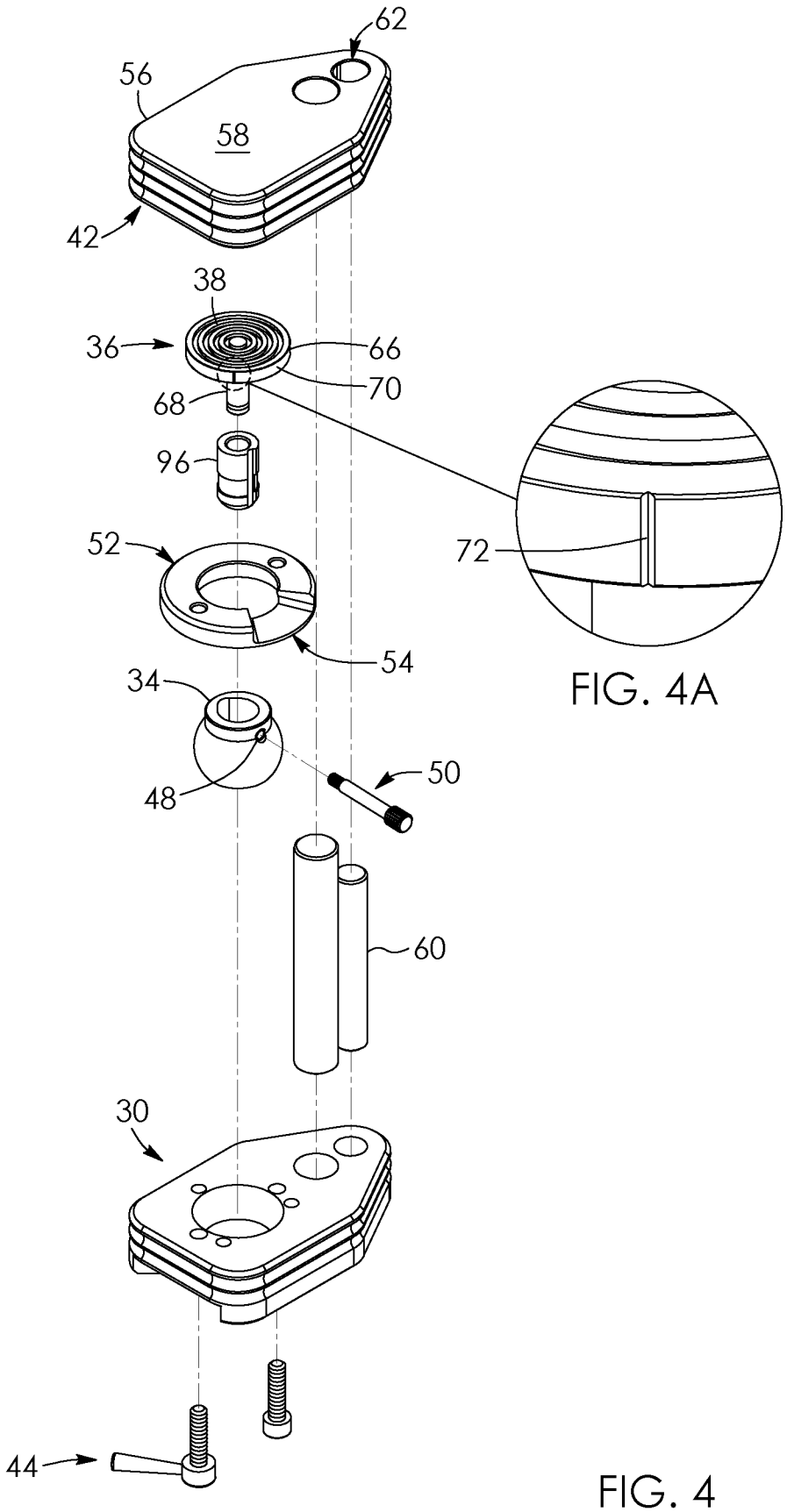


FIG. 4A

FIG. 4

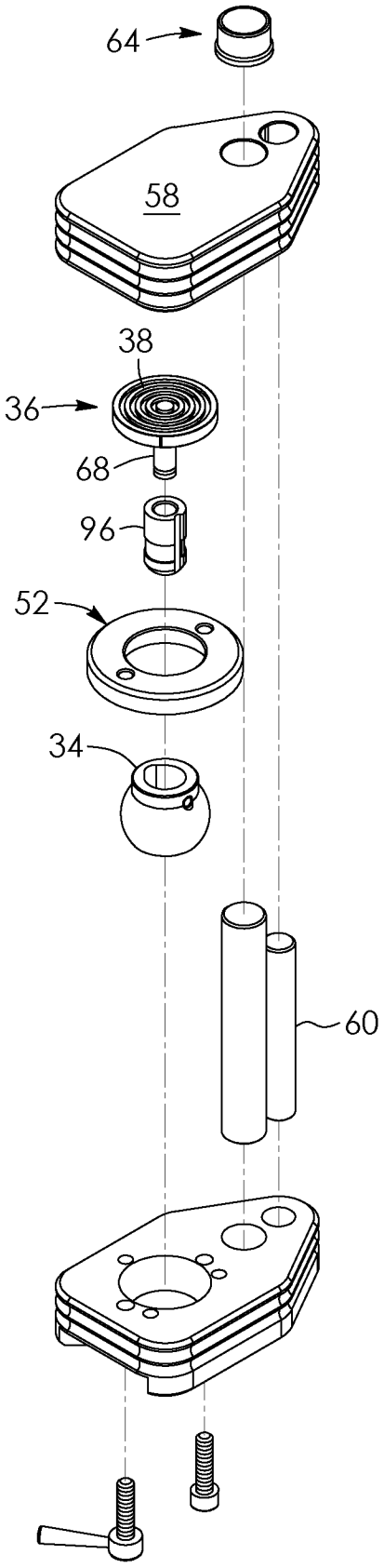


FIG. 4B

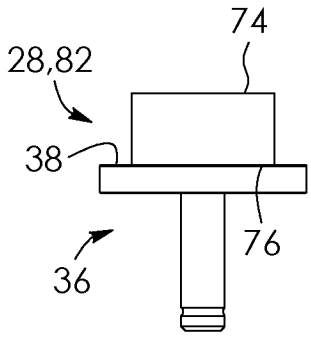


FIG. 5A

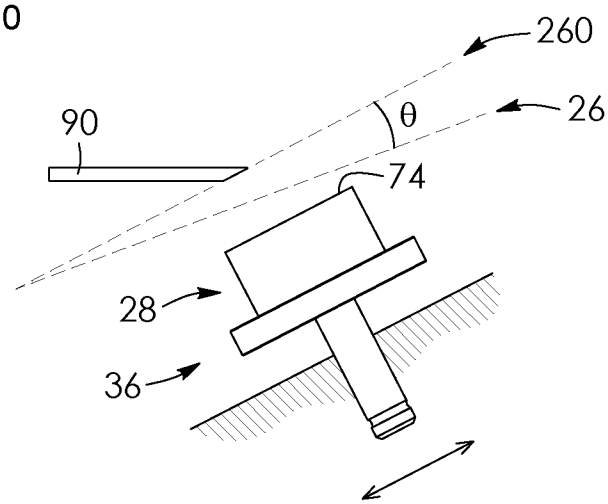


FIG. 5B

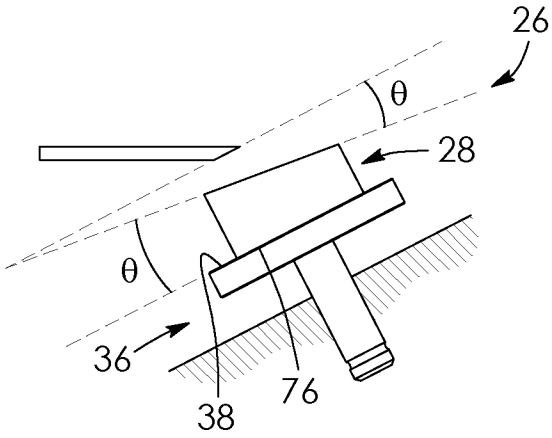


FIG. 5C

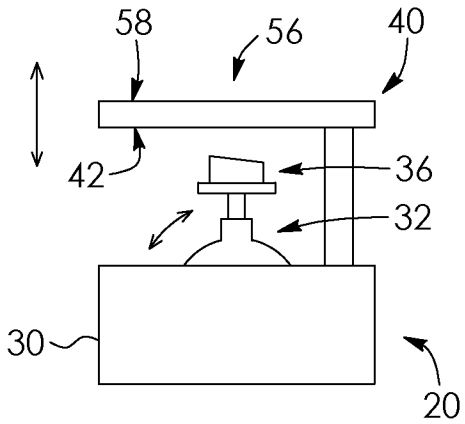


FIG. 5D

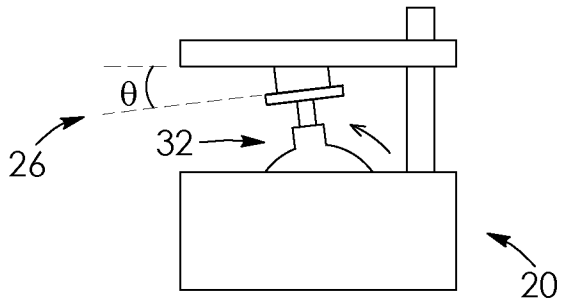


FIG. 5E

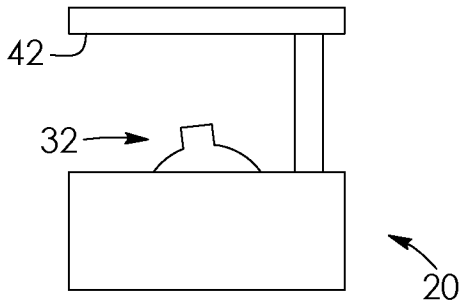


FIG. 5F

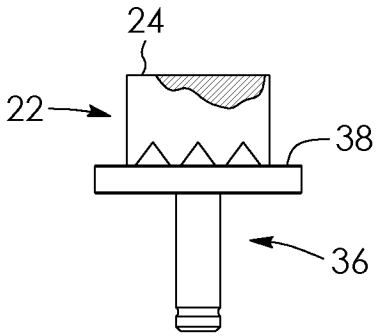


FIG. 5G

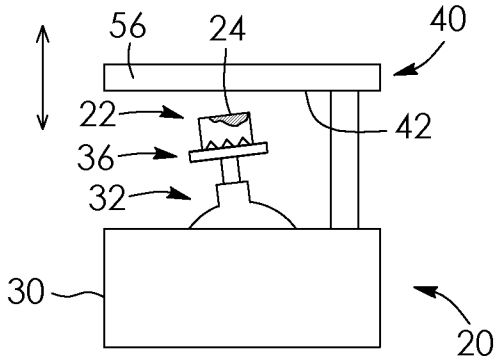


FIG. 5H

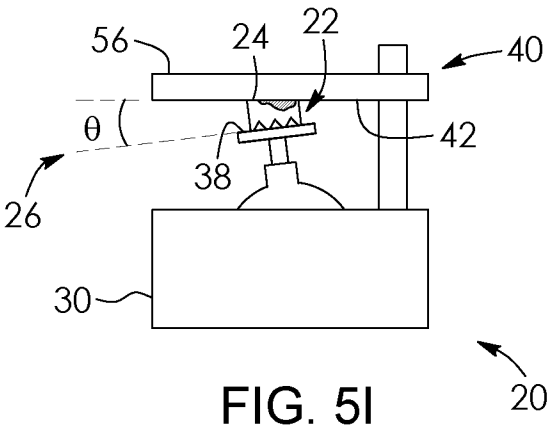


FIG. 5I

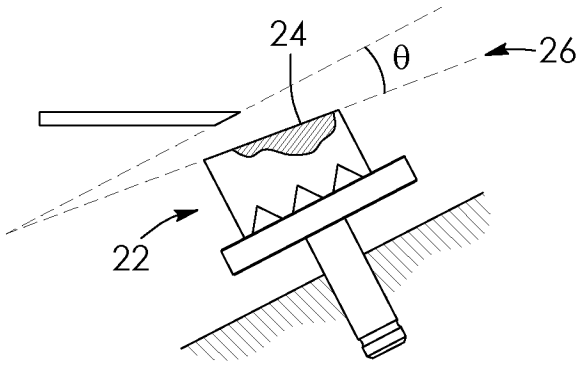


FIG. 5J

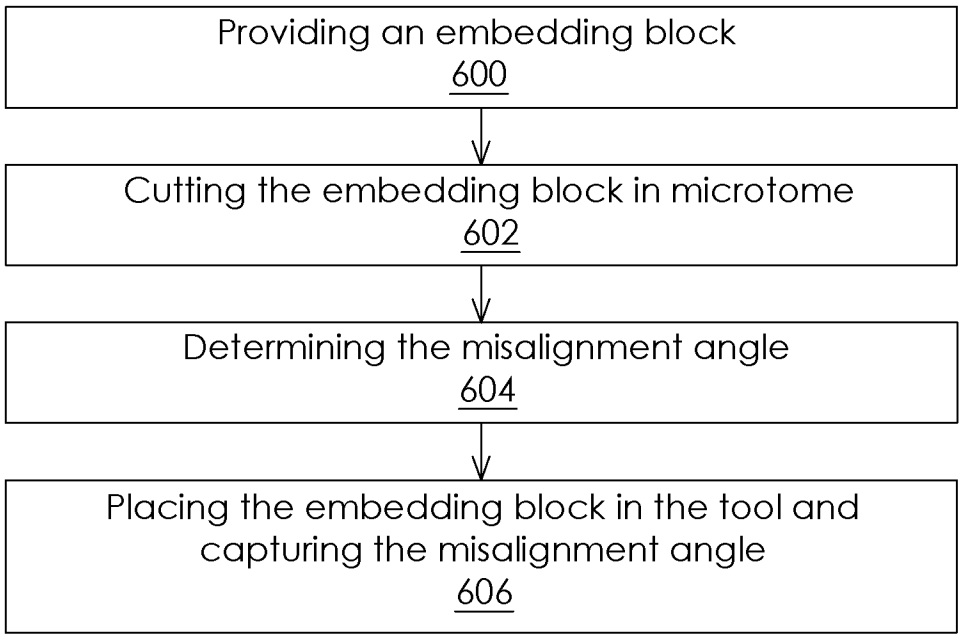

Providing an embedding block
600
Cutting the embedding block in microtome
602
Determining the misalignment angle
604
Placing the embedding block in the tool and capturing the misalignment angle
606

FIG. 6A

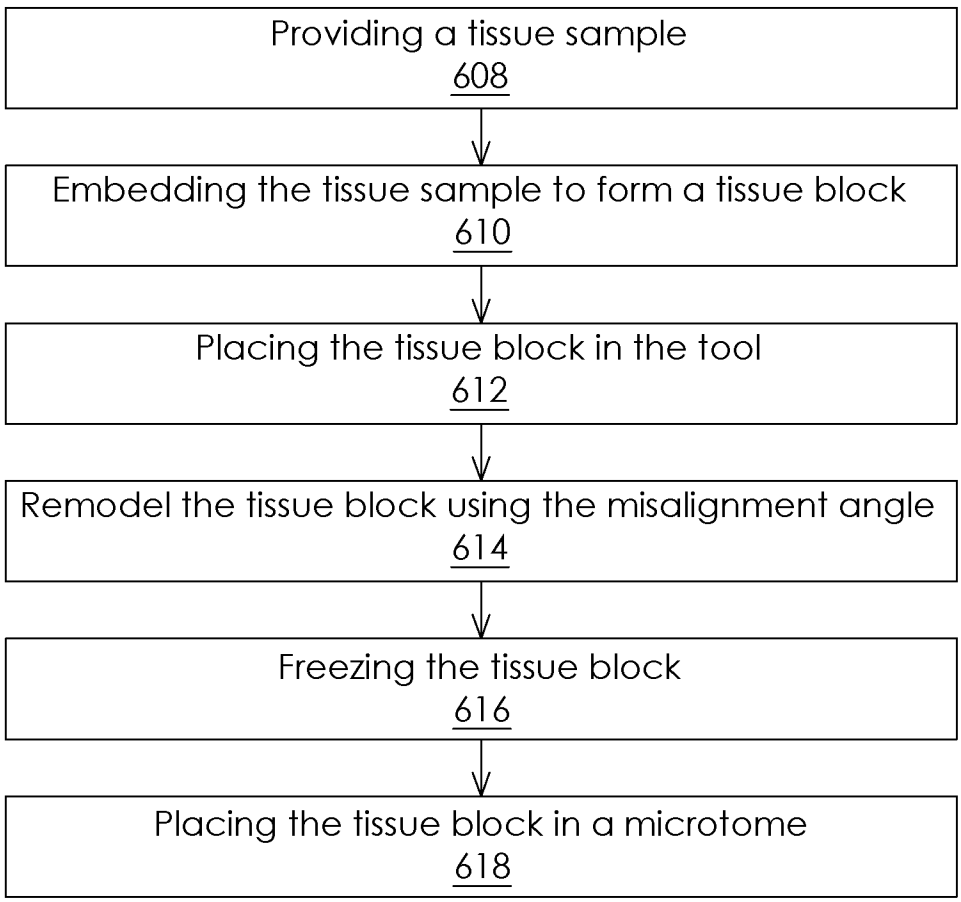

Providing a tissue sample
608
Embedding the tissue sample to form a tissue block
610
Placing the tissue block in the tool
612
Remodel the tissue block using the misalignment angle
614
Freezing the tissue block
616
Placing the tissue block in a microtome
618

FIG. 6B

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2014/051255

A. CLASSIFICATION OF SUBJECT MATTER
IPC: ***G01N 1/06*** (2006.01), ***A61B 10/02*** (2006.01), ***A61B 17/32*** (2006.01), ***A61B 17/3205*** (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G01N (2006.01), A61B (2006.01)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
Google, Google Scholar and Questel Orbit

Keywords: microtome, calibration, angle, embedding block, tissue block, compensation, slice and similar terms.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2012/0240737 (Yang et al.) 27 September 2012 (27-09-2012)	1-18
A	US 8,001,876 (Tabb et al.) 23 August 2011 (23-08-2011)	1-18
A	EP 0 937 975 (Temple et al.) 25 August 1999 (25-08-1999)	1-18
A	US 2008/0022831 (Watanabe et al.) 31 January 2008 (31-01-2008)	1-18
A	US 3,733,948 (Pickett) 22 May 1973 (22-05-1973)	1-18

☐ Further documents are listed in the continuation of Box C.

☑ See patent family annex.

*	Special categories of cited documents:
"A"	document defining the general state of the art which is not considered to be of particular relevance
"E"	earlier application or patent but published on or after the international filing date
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O"	document referring to an oral disclosure, use, exhibition or other means
"P"	document published prior to the international filing date but later than the priority date claimed
"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&"	document member of the same patent family

Date of the actual completion of the international search 04 March 2015 (04-03-2015)	Date of mailing of the international search report 12 March 2015 (12-03-2015)
Name and mailing address of the ISA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001-819-953-2476	Authorized officer Arthur Winnik (819) 934-7880

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CA2014/051255

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
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		US8869666B2	28 October 2014 (28-10-2014)
		AU2012200721A1	11 October 2012 (11-10-2012)
		AU2012200721B2	13 November 2014 (13-11-2014)
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		EP2503315A2	26 September 2012 (26-09-2012)
		EP2503315A3	02 January 2013 (02-01-2013)
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		US2015013512A1	15 January 2015 (15-01-2015)
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		US2011283850A1	24 November 2011 (24-11-2011)
		US8074545B1	13 December 2011 (13-12-2011)
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