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(54) **SYSTEM, METHOD, AND COMPUTER-ACCESSIBLE MEDIUM FOR FABRICATION MINIATURE ENDOSCOPE USING SOFT LITHOGRAPHY**

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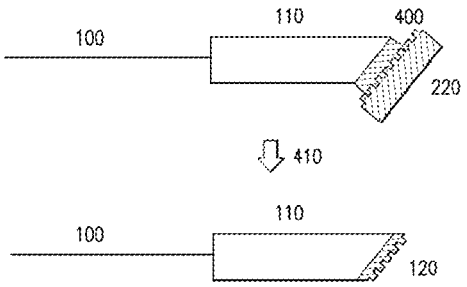
(57) **ABSTRACT**

Exemplary method and system can be implemented and/or used for providing a diffractive configuration in an optical arrangement can be provided. For example, an elastomeric material can be provided with at least one patterned surface. The elastomeric material can be connected with at least one portion of a waveguide arrangement using a pre-polymer adhesive composition. Further, the pre-polymer adhesive composition can be caused to polymerize so as to form the diffractive configuration which at least approximately replicate a structure or at least one feature of an elastomeric mold.

10 Claims, 12 Drawing Sheets



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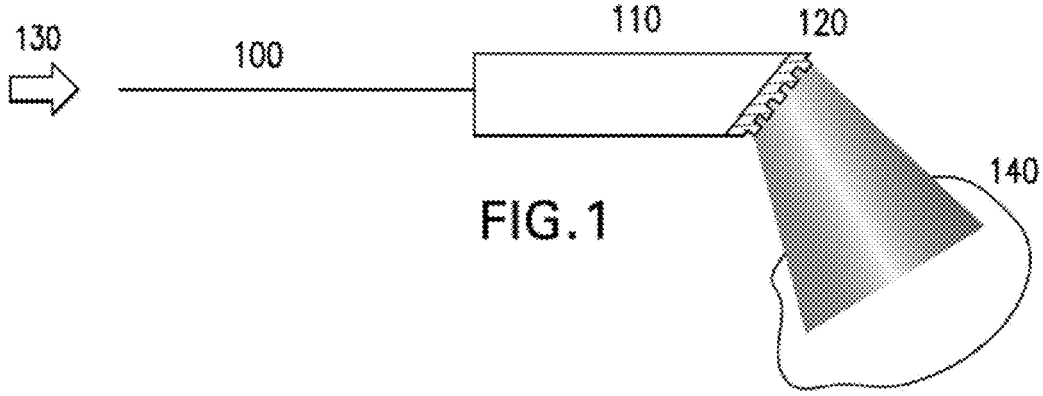

FIG. 1

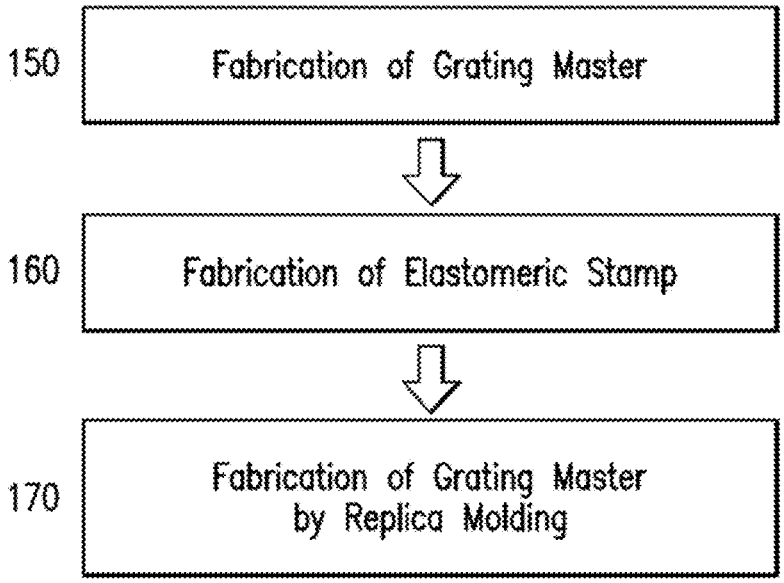
150
Fabrication of Grating Master
160
Fabrication of Elastomeric Stamp
170
Fabrication of Grating Master
by Replica Molding

FIG. 2

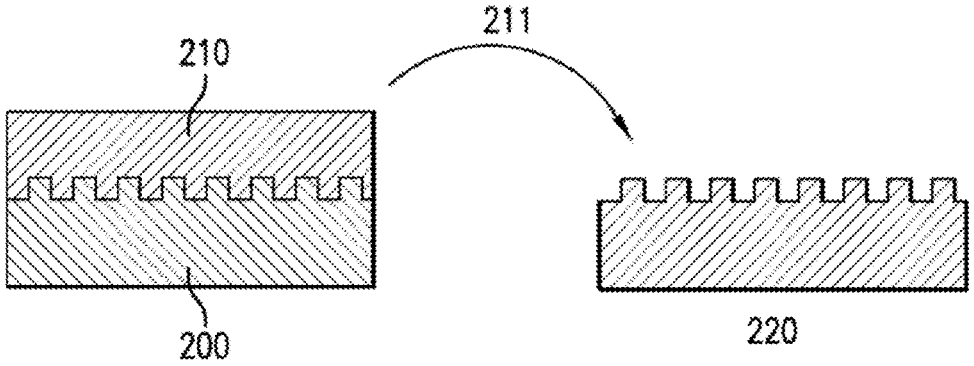

FIG.3

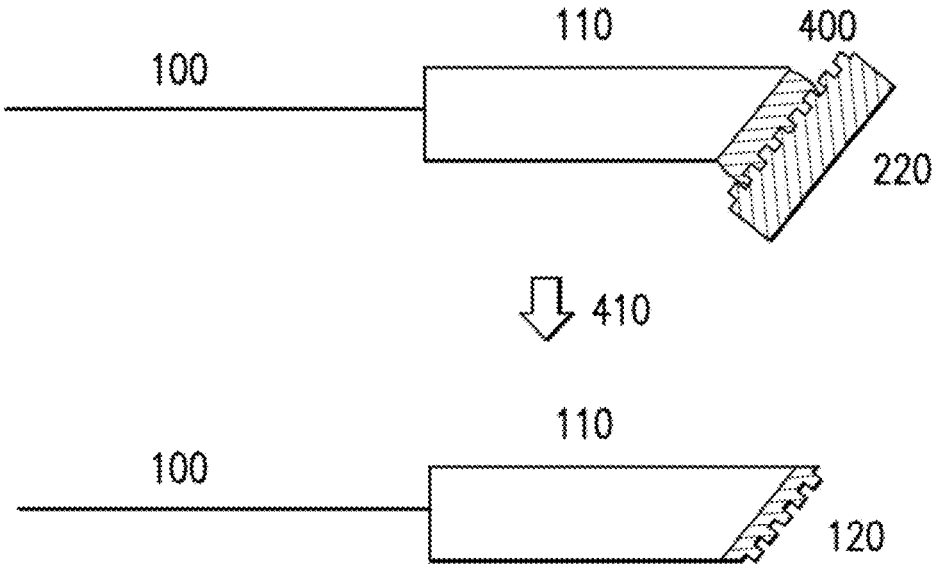

FIG.4

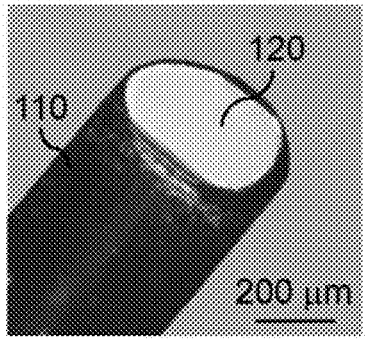

FIG.5A

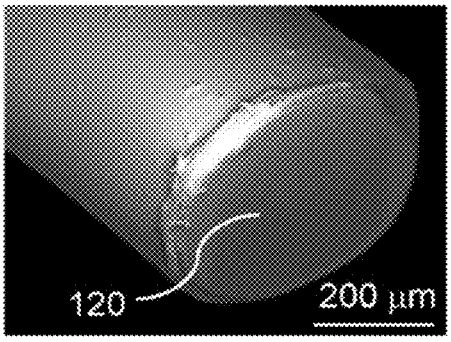

FIG.5B

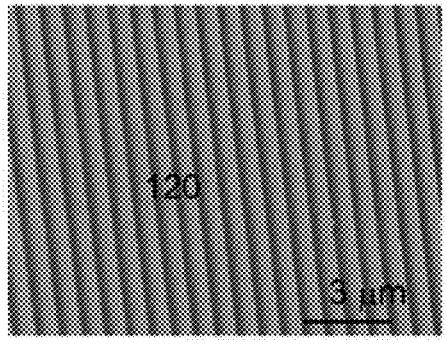

FIG.5C

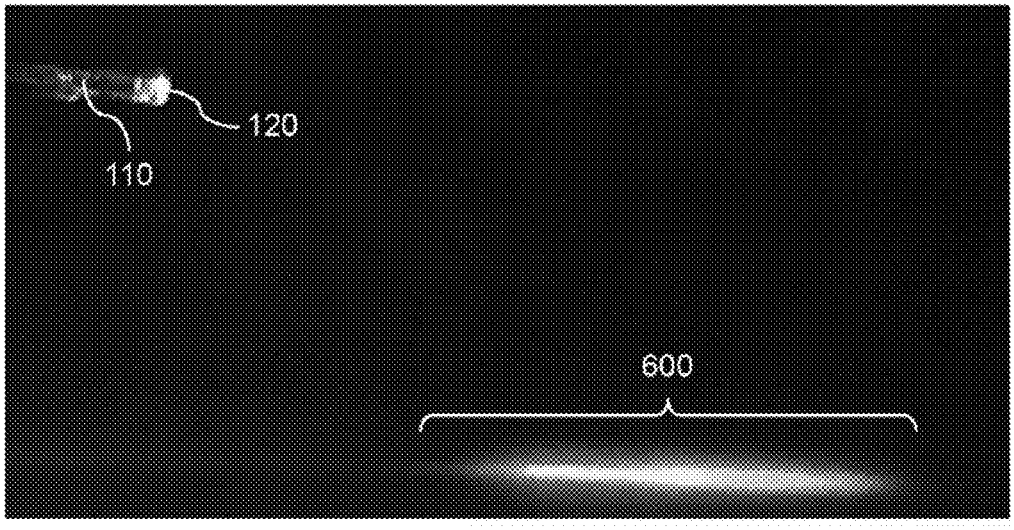

FIG.6

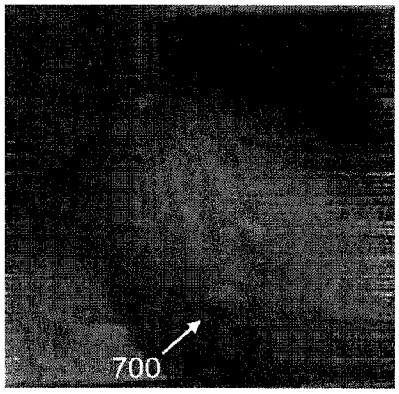

FIG. 7A

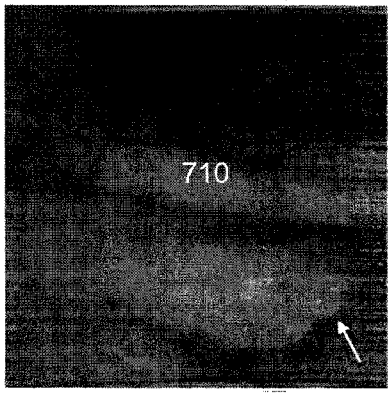

FIG. 7B

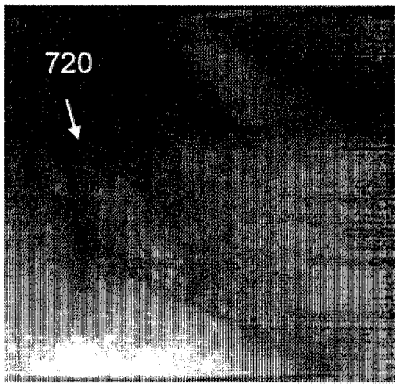

FIG. 7C

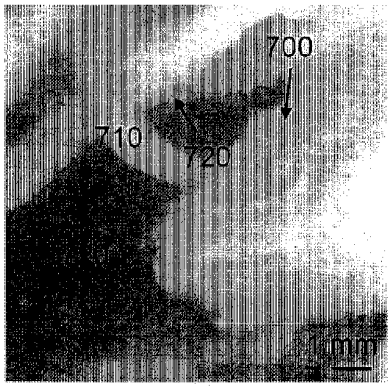

FIG. 7D

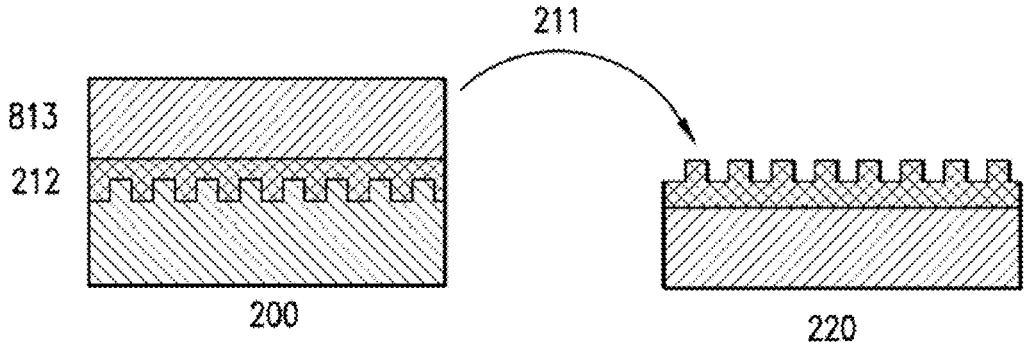

FIG.8

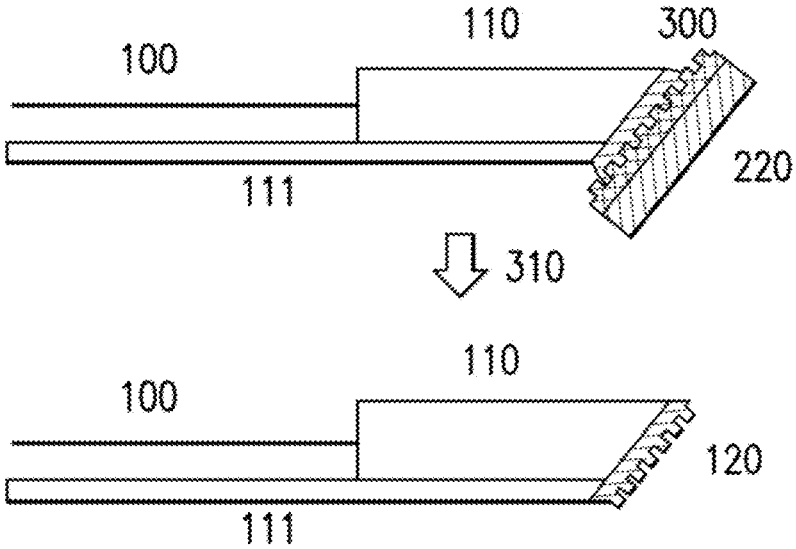

FIG.9

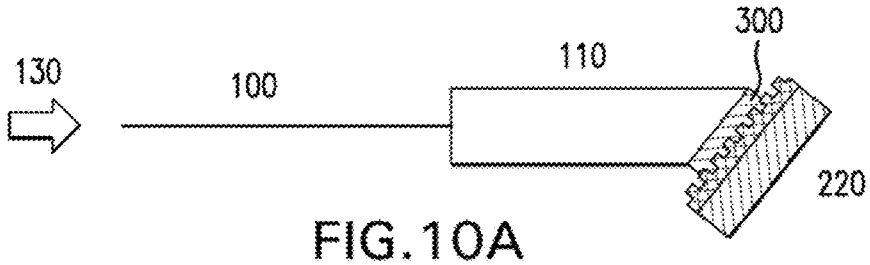

FIG.10A

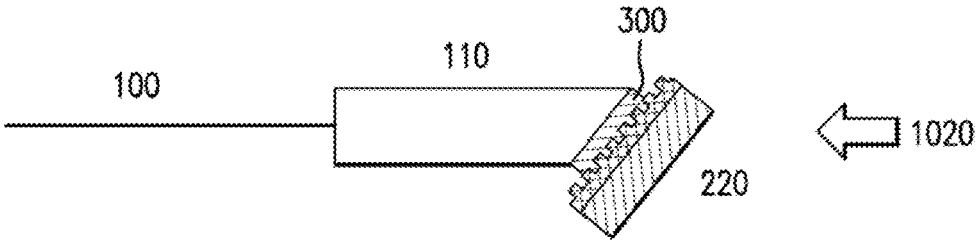

FIG.10B

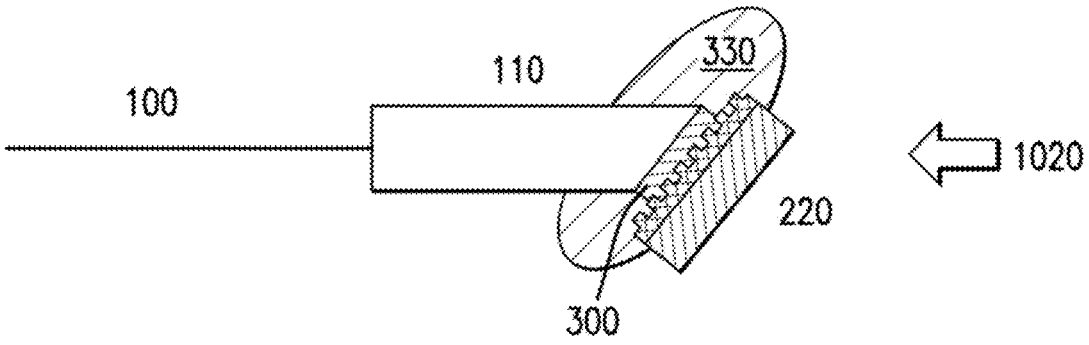

FIG. 11

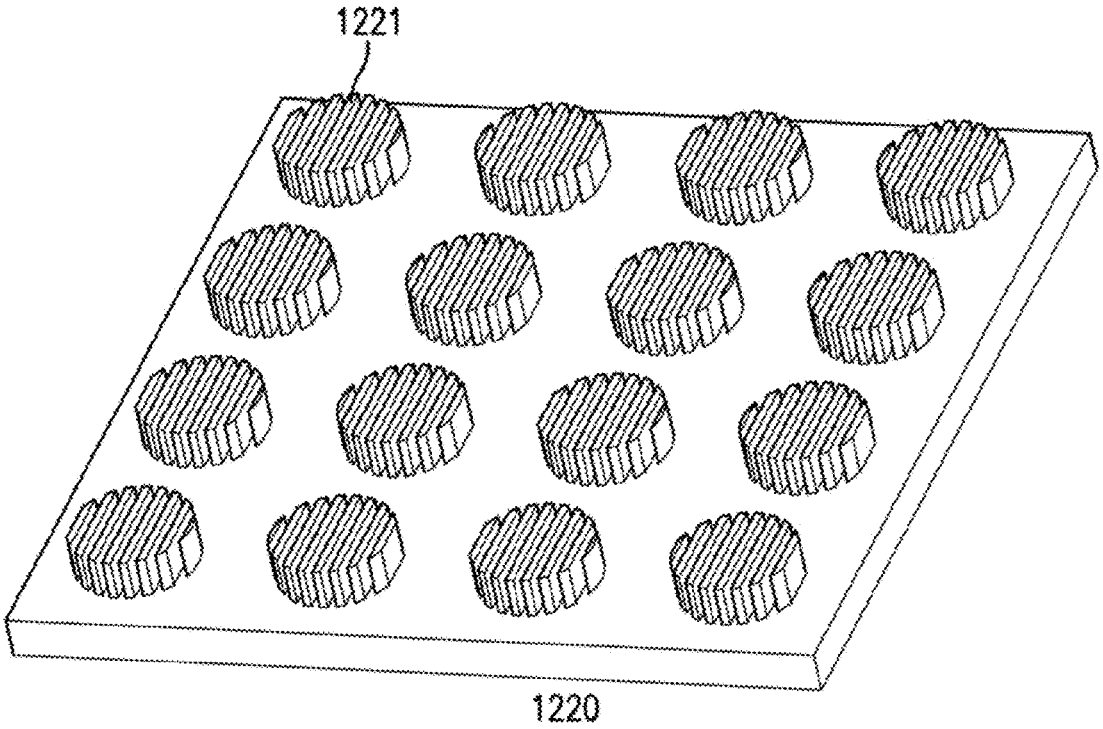

FIG. 12

SYSTEM, METHOD, AND COMPUTER-ACCESSIBLE MEDIUM FOR FABRICATION MINIATURE ENDOSCOPE USING SOFT LITHOGRAPHY

CROSS-REFERENCE TO RELATED APPLICATION(S)

The present application relates to and claims priority from U.S. Provisional Patent Application Ser. No. 61/692,117 filed Aug. 22, 2012 and from U.S. Provisional Patent Application Ser. No. 61/779,671 filed Mar. 13, 2013, the disclosures of which are incorporated herein by reference in their entireties.

FIELD OF THE DISCLOSURE

The present disclosure relates generally to a fabrication of a miniature microscope, and more particularly to exemplary system, method, and computer-accessible medium for fabrication of miniature endoscope using soft lithography, and for minimally-invasive imaging and image-guided therapy.

BACKGROUND INFORMATION

Spectrally encoded endoscopy ("SEE") is a miniature endoscopy technology that can conduct high-definition imaging through a sub-mm diameter probe. With SEE, broadband light is diffracted by a grating at the tip of the fiber, producing a dispersed spectrum on the sample. Light returned from the sample is detected using a spectrometer; and each resolvable wavelength corresponds to reflectance from a different point on the sample. Previously, SEE procedures have been demonstrated using a 350 μm diameter probe, which produced high-quality images in two- and three-dimensions. One of the technical challenges for fabricating SEE probes has been to make a sub-mm transmission grating with a high diffraction efficiency and to precisely assemble the miniature grating with other optical components in the probe.

Thus, there may be a need to improve the above-described fabrication of the SEE probes, and to overcome at least some of the deficiencies of the conventional devices.

SUMMARY OF EXEMPLARY EMBODIMENTS

Thus, to address such exemplary need, system, method, and computer-accessible medium for fabrication of miniature endoscope using soft lithography according to exemplary embodiments of the present disclosure can be provided. According to one exemplary embodiment, method, system, and computer accessible medium can be provided for fabricating SEE probes using soft lithography, including a fabrication of miniature diffraction gratings on the SEE imaging optics.

In one exemplary embodiment, the miniature grating can be provided by first making a PDMS grating master pattern and then replicating the grating pattern on the miniature imaging lens. The smallest diameter of the grating fabricated by this method is only limited by the smallest size of the imaging lens, enabling the fabrication of ultraminiature SEE probe, less than 0.1 mm in diameter. And the miniature gratings can be easily fabricated with UV curing epoxy, polyurethanes, or other low-cost polymers making the final device inexpensive.

Thus, according to certain exemplary embodiments of the present disclosure, exemplary method and system can be presented for providing a diffractive configuration in an optical arrangement can be provided. For example, an elastomeric material can be provided with at least one patterned surface. The elastomeric material can be connected with at least one portion of a waveguide arrangement using a pre-polymer adhesive composition. Further, the pre-polymer adhesive composition can be caused to polymerize so as to form the diffractive configuration which at least approximately replicate a structure or at least one feature of an elastomeric mold.

For example, in one exemplary embodiment of the present disclosure, the diffractive configuration can be a grating. The elastomeric material can be removed from the optical arrangement. The optical arrangement can comprise at least one lens in optical communication with the diffractive configuration. The elastomeric material can comprise a hard elastomeric component and a soft back support. The elastomeric material can be provided by applying an elastomeric stamp to form the patterned surface(s). The pre-polymer adhesive composition can be caused to polymerize by applying at least one electro-magnetic radiation to the pre-polymer adhesive composition to be polymerized. The electro-magnetic radiation can be provided via the waveguide arrangement. The pre-polymer adhesive composition can have a refractive index of between 1.3 and 1.7. The diffractive configuration can have a diameter or a cross-section that is smaller than 1 mm. The grating can have (i) a grove density that is larger than 1000 lines per mm and/or (ii) a grove aspect ratio that is larger than 1. The grating can have diffraction efficiency that is larger than 70%. The diffractive configuration can have at least one lens element. The optical arrangement can include a GRIN lens.

These and other objects, features and advantages of the present disclosure will become apparent upon reading the following detailed description of exemplary embodiments of the present disclosure, when taken in conjunction with the appended drawings and claims.

BRIEF DESCRIPTION OF THE DRAWINGS

Further objects, features and advantages of the disclosure will become apparent from the following detailed description taken in conjunction with the accompanying figures showing illustrative embodiments, results and/or features of the exemplary embodiments of the present disclosure, in which:

FIG. **1** is a schematic diagram of an exemplary SEE probe according to an exemplary embodiment of the present disclosure, fabricated by an exemplary method according to an exemplary embodiment of the present disclosure;

FIG. **2** is a flow diagram of an exemplary grating fabrication method according to an exemplary embodiment of the present disclosure;

FIG. **3** is a schematic diagram of an exemplary elastomeric stamp fabrication process according to an exemplary embodiment of the present disclosure;

FIG. **4** is a schematic diagram of an exemplary grating fabrication process according to an exemplary embodiment of the present disclosure;

FIGS. **5**A-**5**C are a set of exemplary microscopy photos of an exemplary SEE probe according to an exemplary embodiment of the present disclosure;

FIG. **6** is an exemplary photograph of the spectrally-encoded illumination by an exemplary SEE probe according to an exemplary embodiment of the present disclosure;

FIGS. **7**A-**7**D are a set of exemplary SEE images of mouse embryos obtained with an exemplary SEE probe according to an exemplary embodiment of the present disclosure;

FIG. **8** is a diagram of an exemplary method of fabricating a composite elastomeric stamp according to an exemplary embodiment of the present disclosure;

FIG. **9** is a set of illustrations of an exemplary SEE probe that has more than one optical component at the distal end according to an exemplary embodiment of the present disclosure;

FIGS. **10**A and **10**B are illustration of exemplary methods of polymerizing UV-curable prepolymer according to an exemplary embodiment of the present disclosure;

FIG. **11** is an illustration of an exemplary method of polymerizing UV-curable prepolymer under nitrogen-rich environment according to an exemplary embodiment of the present disclosure; and

FIG. **12** is an illustration of an exemplary elastomeric stamp with multiple pillars with each pillar having a grating pattern according to an exemplary embodiment of the present disclosure.

Throughout the drawings, the same reference numerals and characters, unless otherwise stated, are used to denote like features, elements, components, or portions of the illustrated embodiments. Similar features may thus be described by the same reference numerals, which indicate to the skilled reader that exchanges of features between different embodiments can be done unless otherwise explicitly stated. Moreover, while the present disclosure will now be described in detail with reference to the figures, it is done so in connection with the illustrative embodiments and is not limited by the particular embodiments illustrated in the figures. It is intended that changes and modifications can be made to the described embodiments without departing from the true scope and spirit of the present disclosure as defined by the appended claims.

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

A schematic of an exemplary embodiment of the SEE probe is shown in FIG. **1** according to an exemplary embodiment of the present disclosure. This exemplary SEE probe can include an optical fiber **100**, a focusing lens **110**, and a diffraction grating **120**. As shown in FIG. **1**, a broadband light or a UV light **130** can be dispersed along a transverse aspect of the sample **140**.

In one exemplary embodiment of the present disclosure, the diffraction grating **120** can be fabricated based on the exemplary process according to an exemplary embodiment of the present disclosure, as shown in FIG. **2**. In this exemplary process, a master with a grating pattern can be fabricated (procedure **150**). The grating master can be made by various methods, including, e.g., electron-beam lithography, photolithography, interference lithography, nanoembossing, nanoimprint, or reactive ion etching. The exemplary geometry of the grating master can be determined by a numerical simulation to provide high diffraction efficiency at the working spectrum. For example, for the working spectrum of 400-700 nm, the grating can have the groove density of 1379 lines/mm and the groove depth of 1 μm to provide a diffraction efficiency of 85% when the refractive index of the grating material is about 1.47. The grating master can be an etched fused silica grating. Once the grating master is fabricated, an elastomeric stamp can be made (procedure **160**), e.g., using the grating master. The final grating can be made by replica molding of the elastomeric stamp (procedure **170**).

FIG. **3** shows an exemplary diagram of a process of fabricating the elastomeric stamp according to an exemplary embodiment of the present disclosure. For example, a prepolymer **210** can be applied on a grating master **200**. The prepolymer **210** can be cured, thus, e.g., forming an elastomeric material **211**, and peeled off to complete the elastomeric stamp with a grating pattern **220**. The elastomeric stamp can be made of; e.g., Polydimethylsiloxane (PDMS). An example of PDMS can be Sylgrad 184 by Dow Corning. Other elastomers, silicone based polymers, rubbers, or latex derivatives can also be used as stamps. The prepolymer **210** used as a stamp can be cured by heat, catalytic reaction with chemicals or moisture, and/or electromagnetic radiation.

FIG. **4** shows an exemplary illustration of a process of fabricating a miniature grating at the tip of the SEE probe optics, according to an exemplary embodiment of the present disclosure. For example, a prepolymer **400** can be placed at the tip of the focusing lens **110**. The elastomeric stamp with the grating pattern **220** can come into contact with the prepolymer **400**. The prepolymer can be polymerized **410** to complete the miniature grating **120**. The elastomeric stamp **220** can be removed once the miniature grating is completed. The prepolymer **300** can be cured by heat, moisture, and/or electromagnetic radiation. The refractive index of the miniature grating **120** in conjunction with the grating geometry determines the diffraction efficiency. Therefore, the prepolymer **400** can be carefully selected so that the refractive index of the miniature grating **120** can be close to the design refractive index that provides a high diffraction efficiency.

FIG. **5**A depicts an exemplary highly magnified photograph of a tip of an exemplary SEE probe fabricated by the method according to an exemplary embodiment of the present disclosure. The central elliptical region at the distal tip of the SEE probe is green because the grating formed at the probe's tip diffracted the illumination light of the microscope system and preferentially directed the green light to the microscope camera at this particular viewing angle. The area of the green region indicated the area where the miniature grating was well formed. Approximately 86% of the probe diameter along the long axis of the grating and 78% along the short axis showed the green diffraction pattern. A scanning electron microscope (SEM) image (see, e.g., FIG. **5**B) of the SEE probe was acquired with a Zeiss Supra55 VP FESEM at 2 kV at a working distance of 6 mm. Before SEM imaging, the exemplary SEE probe was placed on a silicon wafer and sputter coated with Pt/Pd at 60 mA for 15-45 seconds in order to improve the contrast of the image. The high-magnification SEM image reveals the regular line pattern of the grating (see, e.g., FIG. **5**C). The standard deviation of the groove pitch was measured to be about 1.2% of the mean grating pitch.

A diffraction performance of the exemplary miniature grating **120** shown in FIG. **1** was tested. The exemplary SEE probe generated the spectrally-encoded illumination pattern **600**, which appears as a linear rainbow (see FIG. **6**). The diffraction efficiency of the +1st order, the intensity of the +1st order divided by the intensity of the input beam, was measured to be about 75% for the beam diameter of about 500 μm and the input wavelength of about 532 nm. This diffraction efficiency is lower than that of the master grating, e.g., about 85%. The grating diameter was smaller than the probe diameter, and therefore a portion of light was not diffracted, which reduced the diffraction efficiency. The difference of the refractive index between the master grating and the replicated grating might have also decreased the diffraction efficiency.

FIGS. **7**A-**7**D show a set of exemplary SEE images of mouse embryos obtained with the exemplary SEE probe fabricated by the method according to an exemplary embodiment of the present disclosure. Mouse embryos were inside a polypropylene 50 ml tube, and the SEE imaging was conducted through an approximately 10 mm thick layer of 3.7% formaldehyde fixative solution. The SEE images (see, e.g.,

FIGS. **7**A-**7**C) facilitate a clear visualization of anatomic features of the embryo, including the head, eye **700**, tail **710** and paws with claws **720**, which are similar to those shown in the photo of the same animal (see, e.g., FIG. **7**D).

One of the advantages of the exemplary fabrication method according to an exemplary embodiment of the present disclosure is that the exemplary SEE probes can be made at a low cost. An exemplary elastomeric stamp (e.g., effective grating area=13.5 mm by 12.5 mm) can be used to fabricate approximately 170 miniature gratings assuming that a 1 mm by 1 mm area of the stamp is needed for fabricating an approximately 500-μm-diameter grating. For example, multiple elastomeric stamps can be made without damaging the master. The low cost makes it possible to fabricate cheap and disposable SEE probes, which can facilitate the clinical use of this technology.

It is also advantageous that the exemplary fabrication method according to an exemplary embodiment of the present disclosure can form the miniature grating on the imaging optics as the last step. When the exemplary grating is not properly formed during the fabrication process or is damaged during the use, the tip of the SEE probe can be easily polished by a very small amount (~20 μm) to remove the damaged grating. Following this exemplary corrective action, a new grating can then be fabricated on the same imaging optics. A procedure for handling and precisely aligning the miniature grating may not be needed in the exemplary method according to an exemplary embodiment of the present disclosure, which makes the exemplary fabrication process easier than would a method requiring an alignment.

Another advantage of the exemplary fabrication method according to an exemplary embodiment of the present disclosure is that the exemplary SEE probe size can be decreased further. For example, an ultraminiature GRIN lens with a diameter of about 80 μm has been recently being developed by GRINtech. The exemplary method according to an exemplary embodiment of the present disclosure can be used to make a grating at the tip of the 80-μm GRIN lens, which can make it possible to consider an ultraminiature SEE probe with a diameter that is smaller than 100 μm. For example, the small diameter of the ultraminiature SEE probe can facilitate imaging of the internal tissues that are not currently accessible by the conventional endoscopic imaging devices.

The exemplary elastomeric stamp can be made of two different materials, e.g., to improve the resolution of the replica molding process. FIG. **8** shows an exemplary embodiment of the method according to an exemplary embodiment of the present disclosure that can be used to fabricate a composite elastomeric stamp. In this exemplary embodiment shown in FIG. **8**, an elastomeric prepolymer **212** that can have high stiffness after curing may be placed on the grating master **200**. An example of the elastomer with a high stiffness can be h-PDMS. Then, another elastomeric prepolymer **813** that can have lower stiffness than the first elastomeric material **212** may be poured on top of the first elastomeric material **212**. The two elastomeric materials can be cured and peeled off to complete the final elastomeric stamp **220**.

This exemplary embodiment can be advantageous in replicating a grating pattern with a high aspect ratio. If the elastomeric stamp **220** is made of soft material, such as, e.g., Sylgrad 184, the replicated pattern can collapse and/or sag if the grating pattern has a high aspect ratio. This exemplary composite stamp **220** can combine the advantages of both a more rigid layer **212** (e.g., to achieve high-resolution-pattern transfer) and a more flexible support **213** (e.g., to facilitate a conformal contact with a surface without external pressure).

FIG. **9** shows a set of illustrations of the exemplary SEE probe according to an exemplary embodiment of the present disclosure. In this exemplary embodiment, the distal optics has more than one optical component. For example, light and/or other electro-magnetic radiation from the fiber **100** can be focused by a focusing lens **110**, and light and/or other electro-magnetic radiation from the sample can be collected by an additional fiber, e.g., a detection fiber **111**. The focusing lens **110** and the detection fiber **111** can be assembled before the fabrication of the grating. Then the prepolymer **300** can be both the focusing lens **110** and detection fiber **111** and cured **310** to complete the miniature grating **120**. The method described in this invention can be used for any imaging optics of a range of designs, regardless of the number and dimension of the optical components used.

According to another exemplary embodiment of the SEE probe of the present disclosure, the prepolymer can be UV-curable prepolymer. The UV-curable prepolymer can be cured by various approaches, including those as shown in the exemplary illustration of FIG. **10**. For example, as illustrated in FIG. **10**A, the UV light **130** can be provided and/or coupled to the fiber **100**. In this exemplary embodiment, the area of the prepolymer **300** that is polymerized can be confined to the size of, e.g., the probe diameter. However, when the coupling efficiency of the UV curing light **320** into the fiber **100** is low, the curing time can become long. In FIG. **10**B, the UV light **320** is delivered from the back side of the elastomeric stamp **220**. In this exemplary approach, the curing can be conducted quickly. However, if the prepolymer spreads to an area that is bigger than the probe diameter, the size of the miniature grating can be bigger than the probe diameter.

In another exemplary embodiment of the SEE probe according to the present disclosure as shown in FIG. **11**, the curing can be conducted under nitrogen-rich environment. For example, nitrogen **330** can be provided to the surrounding area of the prepolymer **300**. The nitrogen can prevent the contact between the oxygen and the prepolymer **300**, which can improve the quality of the miniature grating.

In another exemplary embodiment according to the present disclosure, the elastomeric stamp **1220** can be made with multiple circular pillars, as shown in FIG. **12**. For example, each pillar **1221** can have the grating pattern at the top, and the diameter of each pillar is same to the imaging optics diameter. This exemplary stamp can ensure and/or facilitate that the epoxy does not spread behind the diameter of the imaging optics and can make it easy to achieve a circular epoxy spread with a diameter same to the imaging optics diameter.

The foregoing merely illustrates the principles of the invention. Various modifications and alterations to the described embodiments will be apparent to those skilled in the art in view of the teachings herein. Indeed, the arrangements, systems and methods according to the exemplary embodiments of the present invention can be used with any OCT system, OFDI system, SD-OCT system or other imaging systems, and for example with those described in International Patent Application PCT/US2004/029148, filed Sep. 8, 2004, U.S. patent application Ser. No. 11/266,779, filed Nov. 2, 2005, and U.S. patent application Ser. No. 10/501,276, filed Jul. 9, 2004, the disclosures of which are incorporated by reference herein in their entireties. It will thus be appreciated that those skilled in the art will be able to devise numerous systems, arrangements and methods which, although not explicitly shown or described herein, embody the principles of the invention and are thus within the spirit and scope of the present invention. In addition, to the extent that the prior art knowledge has not been explicitly incorporated by reference herein above, it is explicitly being incor-

porated herein in its entirety. All publications referenced herein above are incorporated herein by reference in their entireties.

What is claimed is:

1. A method for providing a diffractive configuration in an optical arrangement, comprising:

providing an elastomeric material with at least one patterned surface;

connecting the elastomeric material with at least one portion of a waveguide arrangement using a pre-polymer adhesive composition; and

causing the pre-polymer adhesive composition to polymerize so as to form the diffractive configuration which at least approximately replicates a structure or at least one feature of the elastomeric material.

2. The method according to claim **1**, wherein the diffractive configuration is a grating, or has at least one of (i) a diameter or a cross-section that is smaller than 1 mm, or (ii) at least one lens element.

3. The method according to claim **1**, further comprising removing the elastomeric material from the optical arrangement.

4. The method according to claim **1**, wherein the optical arrangement comprises at least one lens in optical communication with the diffractive configuration.

5. The method according to claim **1**, wherein the elastomeric material comprises a hard elastomeric component and a soft back support.

6. The method according to claim **1**, wherein the causing procedure includes applying at least one electro-magnetic radiation to the pre-polymer adhesive composition to be polymerized.

7. The method according to claim **6**, wherein the at least one electro-magnetic radiation is provided via the waveguide arrangement.

8. The method according to claim **1**, wherein the pre-polymer adhesive composition has a refractive index of between 1.3 and 1.7.

9. The method according to claim **2**, wherein the grating has at least one of (i) a grove density that is larger than 1000 lines per mm, (ii) a grove aspect ratio that is larger than 1, or (iii) a diffraction efficiency that is larger than 70%.

10. The method according to claim **1**, wherein the optical arrangement includes a GRIN lens.

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