Sapphire-based medical instruments for diagnosis, surgery and therapy

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ABSTRACT

In this work, we present a brief overview of sapphire medical instruments. Sapphire demonstrates a unique combination of physical properties, such as high hardness and chemical inertness, biocompatibility and high thermal conductivity, high transparency in a wide spectral range that makes it suitable for various medical applications. We demonstrate the examples of scalpel, capillary needle for laser therapy, neuroprobe and applicator for cryosurgery. Each of them combines different modalities in one instrument. Among them are tissue resection, therapy via electromagnetic wave delivering, aspiration, diagnosis, and tissue freezing. Sapphire instruments can be accompanied with magnetic resonance imaging and allow multiple sterilization.

Keywords: sapphire shaped crystals, medical instruments, tissue exposure to light, laser thermal therapy, photodynamic therapy, cryosurgery, optically-controlled tissue resection, Edge-defined Film-fed Growth (EFG)

1. INTRODUCTION

Sapphire demonstrates a unique combination of physical properties.[1, 2] It features high hardness, thermal conductivity, significant chemical inertness, thermal stability and high melting point; moreover, it is transparent or translucent for electromagnetic waves in a wide spectral range.[3–5] Biocompatibility of sapphire, impressive waveguiding properties, the ability to operate in contact with biological tissues and liquids, along with the aforementioned properties, makes it rather promising material for designing of medical instruments.

Sapphire crystals with complex shape, often having internal hollow channels, provide different combinations of medical modalities:

- electromagnetic wave delivering to the object using the waveguiding properties of a crystal itself or optical fibers placed inside their channels;
- tissue exposure to electromagnetic radiation;
- surgical resection of tissues;

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- aspiration of tissues;
- laser-assisted thermal destruction;
- cryosurgery of tissues;
- application of the sapphire instruments during magnetic resonance imaging (MRI) of tissues.

Two or more of these properties can be combined in a single instrument. In this work, we overview the promising sapphire instruments for medicine, demonstrate some examples, and discuss their advantages.

2. SAPPHIRE SHAPED CRYSTALS FOR MEDICINE

Due to the high hardness and anisotropy of sapphire, there is a challenging technological problem of making sapphire instruments with complex shape by means of mechanical processing. This limitation is successfully overcame by application of sapphire shaped crystal growth based on the Edge-defined Film-fed Growth (EFG) and related techniques.[6–8] This method is based on the crystal growth from an Al_2O_3-film melt, which is formed on the top of a die with one or more capillary channels at the temperature of 2053 °C in an ambient high-purity Ar-atmosphere. It needs

- an induction-heated graphite susceptor;
- a molybdenum crucible;
- a Verneuil crystal as a feed material.

The design of a die determines the further form and shape of a crystal. More information about this approach can be found in Refs.[2,9–11] We should note that applying the precise crystal weight measurements during growth process,[12] it is possible to significantly improve the crystal quality and produce crystals with as-grown optically-smoothed surfaces. EFG-grown crystals can have one or more internal channels, various cross-sections, such as cylinder or ribbon, and different tips; they do not need significant additional mechanical processing.

EFG technique is applied for making sapphire shaped cylinders with one or more internal hollow channels parallel to the cylinder's axis. Thin needle capillaries, for example, can have internal channel with diameter of ~ 500 μm. The channel can be closed from the one side of a needle capillary, in this case its end takes the semi-spherical form and is determined by the crystal growth process as well as the capillary tip's form. Additional processing of the tips can be performed by mechanical shaping, if required. At the same time, one can produce sapphire tubes, or multichannel sapphire shape crystals.[13–16]

It is quite challenging to grow sapphire thin ribbons with hollow capillary channels due to the difficulty of maintenance the complex thermal conditions at the meniscus, which are necessary for rather small diameter of the channel. Nevertheless, a special design of a molybdenum die effectively solve this problem.[17–19] Such ribbons with internal channels closed at the one side are used for producing of sapphire scalpels. Its blade is made by means of mechanical grinding and polishing. In several cases, it is required to produce sapphire cylinder with different segments, hollow or monolithic without mechanical shaping; for this purpose the Non-Capillary Shaping Technique is used.[20]

3. SAPPHIRE MEDICAL INSTRUMENTS

The examples of sapphire instruments are shown in Fig. 1. Among them are neuroprobe for intraoperative diagnosis, aspiration and coagulation of tissues, diagnostic scalpel that enables coagulation of blood vessels, needles for interstitial thermotherapy and photodynamic therapy, and applicator for cryosurgery.

The sapphire contact neuroprobe demonstrated in Fig. 1(a) enables intraoperative optical diagnosis of brain malignant tissues via fluorescent analysis, aspiration of tissues, and coagulation of blood vessels.[21,22] It includes one open channel for aspiration and two channels closed near the contact with tissue for placing optical fibers for delivering and receiving laser radiation. Fig. 1(b) demonstrated the detected by the neuroprobe endogenous

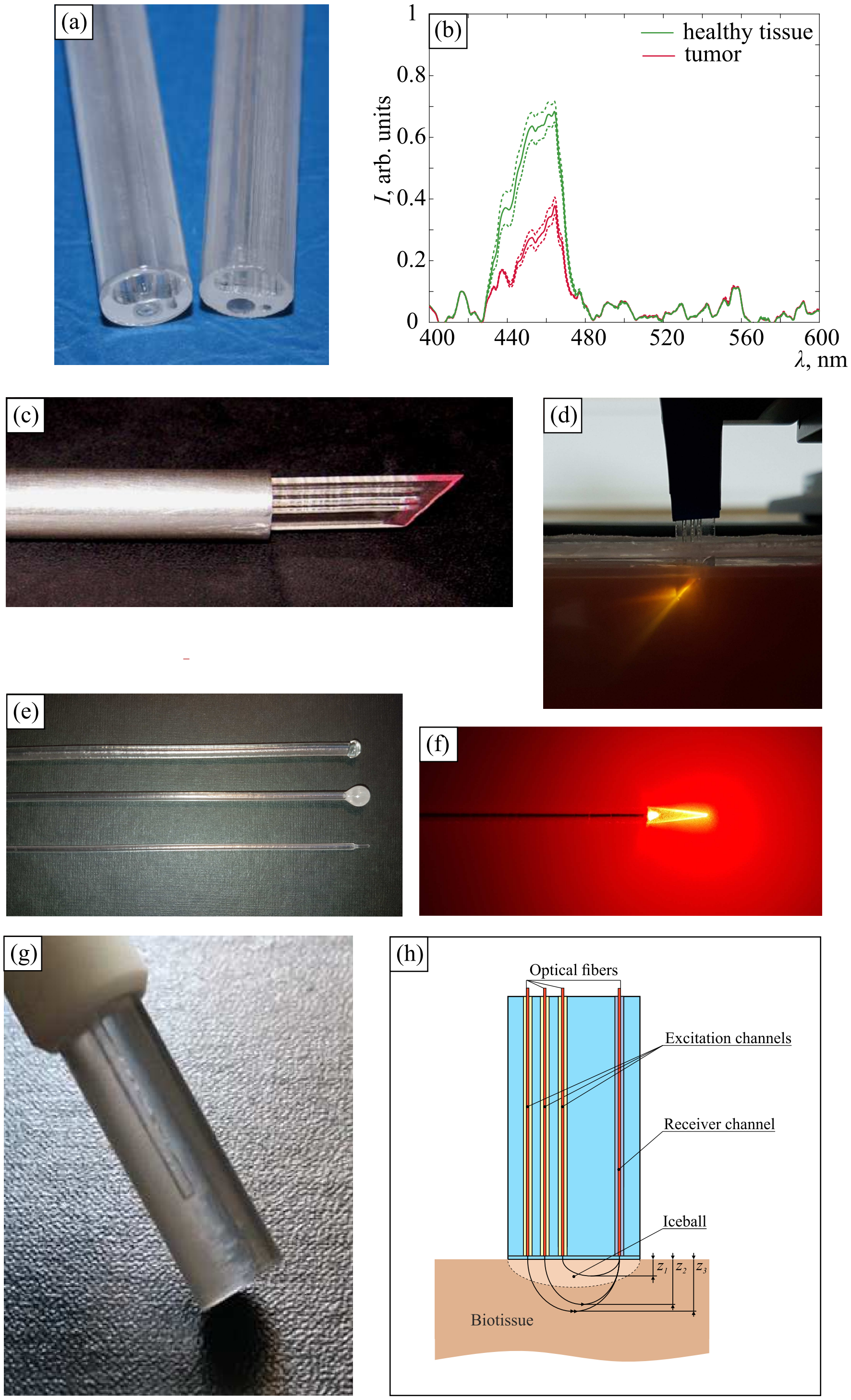

Figure 1. Sapphire medical instruments: (a) diagnostic neuroprobe for aspiration and (b) the fluorescence spectra of rat brain tissues *ex vivo* registered by means of the neuroprobe; (c) sapphire diagnostic scalpel, (d) its application in a model gelatin media containing fluorescent dye; (e) examples of needles for interstitial laser therapy, (f) radiation pattern obtained in an intralipid-based scattering media; (g) applicator for cryosurgery, (h) a scheme for sapphire cryoapplicator with optical diagnosis of freezing front in tissues.

fluorescent signal (excitation is at the wavelength $\lambda = 365\ nm$) from the *ex vivo* rat brain tissues, i.e. healthy tissue (cortex) and tumorous (glioma model). The differences between the received signals are clearly observed. It should be noted that the sapphire neuroprobe can be combined with other optical diagnostic methods thanks to the high transparency of sapphire in optical range. In case of using optical fibers inside the closed internal channels of sapphire shaped crystals, it is important to note that the fiber is protected from the direct contact with tissues, correspondingly, from its degradation.

Sapphire scalpel demonstrated in Fig. 1(c) enables tissue resection, intraoperative optical diagnosis, and laser coagulation. Two latter modalities are provided by three capillary channels inside the sapphire ribbon. Optical fibers placed inside the channels are used for tissue exposure with diagnostic radiation and laser radiation for coagulation,[23,24] and detection of the fluorescent radiation. The fibers are protected since the channels are closed near the blade. Analysis of the exogenous or endogenous fluorescent signal can help a surgeon to find the borders of the resected malignancies. The radius of a cutting edge of this scalpel can achieve 25 nm; its blade features low friction coefficient and high stability of the cutting edge; repeated sterilization does not damage the blade,[25] therefore such scalpel is reusable.

Fig. 1(d) demonstrates the fluorescence of the gelatin phantom, which contain rhodamine 6G dye. The excitation fiber was connected to the laser diode with the wavelength 465 nm. A strong fluorescent radiation is clearly seen during the immersion of the scalpel inside the phantom.

Fig. 1(e) shows the examples of sapphire needles for interstitial thermal- and photodynamic therapy.[26–29] Sapphire needles for light delivering inside tissues can replace the commonly used approach, which is the introduction of a bare optical fiber into a tissue using removable catheters.[26,30] In case of sapphire needle, there is no need in remove of needles itself, because of high transparency of sapphire and the closed internal capillary channel. Thus, the optical fiber is protected from the contact with tissue and the corresponding chemical damage, which often leads to an additional unpredictable carbonization of tissues.[31] The diameter of a sapphire needle can be less than 1.5 mm and maintain the requirement of low invasiveness; the diameter of internal channel is near or less than 500 μm; the length of the needle can exceed 200 mm. The demonstrated needles have different tips therefore, they can form different radiation patterns inside or at the surface of biological tissues.[32] The radiation pattern obtained by a pointed needle in an intralipid-based scattering media served as a tissue phantom is shown in Fig. 1(f).

Sapphire applicators for cryodestruction of tissues have a number of advantages due to high thermal conductivity of sapphire at cryogenic temperatures. The example of such applicator is shown in Fig. 1(g). It also can be combined with laser source for additional heating or laser therapy by placing optical fiber inside the internal channel of this applicator.[33] A promising scheme of cryoapplicator enabling optical control of tissue freezing is demonstrated in Fig. 1(h). The problem of an intraoperative monitoring of the ice-ball formation is rather challenging and limits the application area of cryosurgery. It can be solved by the proposed method of detecting the diffuse reflected radiation,[34] when several channels for tissue excitation with modulated optical radiation and one receiver channel are used.[35]

4. CONCLUSIONS

In this work we present the sapphire medical instruments that are able to combine different modalities in the one instrument body. The advantages of the EFG and related techniques of sapphire shaped crystal growth allow for making such instruments without significant and expensive mechanical processing. The transparency of sapphire enables tissue exposure and detection of optical radiation, thus, it can be applied for medical diagnosis and therapy. The discussed functions of these instruments are rather wide, therefore, sapphire shape crystals meet the demands of modern trends in medicine.

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REFERENCES

[1] Klassen-Neklyudova, M. V. and Bagdasarov, K. S., [*Ruby and Sapphire*], Nauka, Moscow (1974).

[2] Kurlov, V. N., Rossolenko, S. N., Abrosimov, N. V., and Lebbou, K., [*Crystal Growth Processes Based on Capillarity: Czochralski, Floating Zone, Shaping and Crucible Techniques. Chapter 5. Shaped Crystal Growth (pages 277-354)*], John Wiley & Sons, United Kingdom (2010).

[3] Lacovara, P., Esterowitz, L., and Kokta, M., "Growth, spectroscopy, and lasing of titanium-doped sapphire," *IEEE Journal of Quantum Electronics* **21**, 1614–1618 (Oct 1985).

[4] Grischkowsky, D., Keiding, S., van Exter, M., and Fattinger, C., "Far-infrared time-domain spectroscopy with terahertz beams of dielectrics and semiconductors," *J. Opt. Soc. Am. B* **7**, 2006–2015 (Oct 1990).

[5] Jianwei, X., Yongzong, Z., Guoqing, Z., Ke, X., Peizhen, D., and Jun, X., "Growth of large-sized sapphire boules by temperature gradient technique (TGT)," *Journal of Crystal Growth* **193**(1–2), 123–126 (1998).

[6] LaBelle, H. E. and Mlavsky, A. I., "Growth of controlled profile crystals from the melt: Part I – Sapphire filaments," *Materials Research Bulletin* **6**(7), 571–579 (1971).

[7] LaBelle, H. E., "Growth of controlled profile crystals from the melt: Part II – Edge-defined, film-fed growth (EFG)," *Materials Research Bulletin* **6**(7), 581–589 (1971).

[8] Chalmers, B., LaBelle, H. E., and Mlavsky, A. I., "Growth of controlled profile crystals from the melt: Part III – Theory," *Materials Research Bulletin* **6**(8), 681–690 (1971).

[9] Antonov, P. I. and Kurlov, V. N., "A review of developments in shaped crystal growth of sapphire by the Stepanov and related techniques," *Progress in Crystal Growth and Characterization of Materials* **44**(2), 63–122 (2002).

[10] Abrosimov, N. V., Kurlov, V. N., and Rossolenko, S. N., "Automated control of Czochralski and shaped crystal growth processes using weighing techniques," *Progress in Crystal Growth and Characterization of Materials* **46**(1–2), 1–57 (2003).

[11] Katyba, G., Zaytsev, K., Dolganova, I., Shikunova, I., Chernomyrdin, N., Yurchenko, S., Komandin, G., Reshetov, I., Nesvizhevsky, V., and Kurlov, V., "Sapphire shaped crystals for waveguiding, sensing and exposure applications," *Progress in Crystal Growth and Characterization of Materials* **64**(4), 133 – 151 (2018).

[12] Kurlov, V. N. and Rossolenko, S. N., "Growth of shaped sapphire crystals using automated weight control," *Journal of Crystal Growth* **173**(3–4), 417–426 (1997).

[13] Zaytsev, K., Katyba, G., Kurlov, V., Shikunova, I., Karasik, V., and Yurchenko, S., "Terahertz photonic crystal waveguides based on sapphire shaped crystals," *IEEE Transactions on Terahertz Science and Technology* **6**(4), 576–582 (2016).

[14] Katyba, G., Zaytsev, K., Shikunova, I., Rossolenko, S., Chernomyrdin, N., Karasik, V., Mukhina, E., Reshetov, I., Yurchenko, S., and Kurlov, V., "Terahertz waveguides based on multichannel sapphire shaped crystals," *Proceedings of SPIE* **9993**, 99930I (2016).

[15] Katyba, G. M., Zaytsev, K. I., Rossolenko, S. N., Shikunova, I. A., Shikunov, S. L., Stryukov, D. O., Yurchenko, S. O., and Kurlov, V. N., "Technological aspects of manufacturing terahertz photonic crystal waveguides based on sapphire shaped crystals," *Proceedings of SPIE* **10333**, 103331C (2017).

[16] Katyba, G., Zaytsev, K., Chernomyrdin, N., Shikunova, I., Komandin, G., Anzin, V., Lebedev, S., Spektor, I., Karasik, V., Yurchenko, S., Reshetov, I., Kurlov, V., and Skorobogatiy, M., "Sapphire photonic crystal waveguide for terahertz sensing in aggressive environments," *Advanced Optical Materials* **6**(22), 1800573 (2018).

[17] Kurlov, V. N., Shikunova, I. A., Ryabova, A. V., and Loschenov, V. B., "Sapphire smart scalpel," *Bulletin of the Russian Academy of Sciences: Physics* **73**(10), 1341–1344 (2009).

[18] Shikunova, I. A., Kurlov, V. N., Ryabova, A. V., and Loschenov, V. B., "Sapphire diagnostic scalpel," *Lasers in Medical Science* **24**, S31 (2009).

[19] Kurlov, V. N., Shikunova, I. A., Ryabova, A. V., and Loschenov, V. B., "Sapphire smart scalpel," *AIP Conference Proceedings* **1226**, 76–81 (2010).

[20] Kurlov, V. N., "The noncapillary shaping (NCS) method: a new method of crystal growth," *Journal of Crystal Growth* **179**(1), 168–174 (1997).

[21] Shikunova, I. A., Stryukov, D. O., Rossolenko, S. N., Kiselev, A. M., and Kurlov, V. N., "Neurosurgery contact handheld probe based on sapphire shaped crystal," *Journal of Crystal Growth* **457**, 265–269 (2017).

[22] Shikunova, I., Zaytsev, K., Stryukov, D., Dubyanskaya, E., and Kurlov, V., "Neurosurgical sapphire handheld probe for intraoperative optical diagnostics, laser coagulation and aspiration of malignant brain tissue," *Proceedings of SPIE* **10411**, 104110Q (2017).

[23] Dobrovinskaya, R. E., Litvinov, L. A., and Pishchik, V. V., [*Sapphire: Material, Manufacturing, Applications*], Springer, New York, NY, USA (2009).

[24] Doty, J. L. and Auth, D. C., "The laser photocoagulating dielectric waveguide scalpel," *IEEE Transactions on Biomedical Engineering* **BME-28**(1), 1–9 (1981).

[25] Zhang, D. and Gan, Y., "Recent progress on critical cleaning of sapphire single-crystal substrates: A mini-review," *Recent Patents on Chemical Engineering* **6**(3), 161–166 (2013).

[26] Wilson, B. C. and Patterson, M. S., "The physics, biophysics and technology of photodynamic therapy," *Physics in Medicine and Biology* **53**(9), R61–R109 (2008).

[27] Svanberg, K., Bendsoe, N., Axelsson, J., Andersson-Engels, S., and Svanberg, S., "Photodynamic therapy: superficial and interstitial illumination," *Journal of Biomedical Optics* **15**(4), 041502 (2010).

[28] Bretschneider, T., Ricke, J., Gebauer, B., and Streitparth, F., "Image-guided high-dose-rate brachytherapy of malignancies in various inner organs – technique, indications, and perspectives," *Journal of Contemporary Brachytherapy* **8**(3), 251–261 (2016).

[29] Sharma, M., Balasubramanian, S., Silva, D., Barnett, G. H., and Mohammadi, A. M., "Laser interstitial thermal therapy in the management of brain metastasis and radiation necrosis after radiosurgery: An overview," *Expert Review of Neurotherapeutics* **16**(2), 223–232 (2016).

[30] Keiser, G., Xiong, F., Cui, Y., and Shum, P. P., "Review of diverse optical fibers used in biomedical research and clinical practice," *Journal of Biomedical Optics* **19**(8), 080902 (2014).

[31] Pantaleone, C., Dymling, S., and Axelsson, J., "Optical fiber solutions for laser ablation of tissue and immunostimulating interstitial laser thermotherapy – product development in the network of developers, industry and users," *Photonics & Lasers in Medicine* **5**(1), 69–75 (2015).

[32] Dolganova, I. N., Shikunova, I. A., Katyba, G. M., Zotov, A. K., Mukhina, E. E., Shchedrina, M. A., Tuchin, V. V., Zaytsev, K. I., and Kurlov, V. N., "Optimization of sapphire capillary needles for interstitial and percutaneous laser medicine," *Journal of Biomedical Optics* **24**(12), 128001 (2019).

[33] Shikunova, I. A., Dubyanskaya, E. N., Kuznetsov, A. A., Katyba, G. M., Dolganova, I. N., Mukhina, E. E., Chernomyrdin, N. V., Zaytsev, K. I., Tuchin, V. V., and Kurlov, V. N., "Sapphire shaped crystals for laser-assisted cryodestruction of biological tissues," *Proceedings of SPIE* **10716**, 1071615 (2018).

[34] Tuchin, V., [*Tissue Optics: Light Scattering Methods and Instruments for Medical Diagnosis, Second Edition*], SPIE Press, USA (2007).

[35] Dubyanskaya, E., Chernomyrdin, N., Dolganova, I., Kuznetsov, A., Mukhina, E., Safonova, L., Donodin, A., Shikunova, I., Zaytsev, K., and Kurlov, V., "A concept of cryoapplicator based on sapphire shaped crystal enabling control of the ice ball formation using spatially-resolved elastic backscattering of light," *Proceedings of SPIE* **10685**, 1068529 (2018).