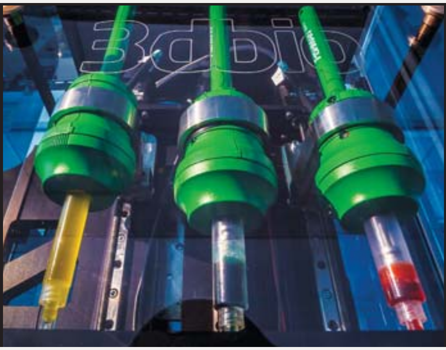
3dbio

3d bioprinting solutions
creating future possibilities

www.bioprinting.ru



FABION

First made in the summer of 2014

Russia's first bioprinter of original design
3D Bioprinting Solutions

investor *www.invitro.ru*
www.centrallabinvitro.com

INVITRO®

partner *www.healthinvestors.ru*

Health Care Capital Group
Venture investments in health care

February 1, 2013 – Biotechnology Research Laboratory foundation (Russia's first private laboratory aimed at the development of 3D bioprinting technology).

February 12, 2013 – Acquisition of The Skolkovo Innovation Center participant certificate and status.

February 14, 2013 – The Regenerative Medicine in Russia international conference emerged as a first international scientific event where bioprinting and biofabrication issues were raised at an expert level for the first time.

March 1, 2013 – INVITRO company invested in the development of human organ bioprinting technology. Construction and equipment procurement for the «3D Bioprinting Solutions» Biotechnology Research Laboratory was launched.

2013

The Biotechnology Research Laboratory is Russia's first private laboratory developing the technology of 3D human organ bioprinting. The laboratory is one of the 16* companies in the world possessing commercially-rated original design bioprinters.

* according to the internal review of 2014

3D Bioprinting Solutions
Biotechnology Research Laboratory

The 3D human organ bioprinting technology has a potential of becoming the savior for the millions of people needing restoration or transplantation of defective or entirely lost organs. As well as that, this technology is a powerful tool for resolving the immune compatibility problems.

The Company was founded in 2013.

The 3D Bioprinting Solutions Biotechnology Research Laboratory is Russia's only privately-owned laboratory developing its proprietary bioprinting technology and possessing a bioprinter of original design. The Laboratory's main investor is INVITRO company.

OUR MISSION

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Development and introduction of 3D human organ bioprinting technology in Russia and abroad

May 2013 — An international multidisciplinary team formed — a quintessence of intellectual potential and experience of world leading experts in the field of regenerative medicine comprising world-class researchers, engineers and managers. By the time of formation, composite service record of the team's researchers was a bit over 50 years.

September 6, 2013 — *3D Bioprinting Solutions* Biotechnology Research Laboratory opened in Moscow. It is a truly ultramodern and innovative establishment.

September 2013 — Research work started and cooperation organized with foreign research teams, who are involved in bioprinting and are experts in material technology and other relevant disciplines and who adhere to the principles of evidence-based medicine, to put together the intellectual potential and unique experiences accumulated in the field of regenerative medicine.

The team of 16 people represents the entire world research community. The Laboratory's general director is Alexander Yurievich Ostrovsky, the founder of the INVITRO brand.

FABION is Russia's first 3D bioprinter of original design made for printing functional human tissues and/or organs, which allows achieving accurate distribution of tissue spheroids (bioinks) in sequential hydrogel layers (biopaper) according to a pre-designed 3D digital model. Thanks to the unique design and engineering solutions developed by 3D Bioprinting Solutions, the new bioprinter is a truly multipurpose tool for printing functional 3D human tissue and organ constructs. FABION's original design and make are based of the proprietary technology of 3D bioprinting. In terms of several performance indicators, FABION is superior to other available bioprinters.

FABION's main advantages and distinctive features:

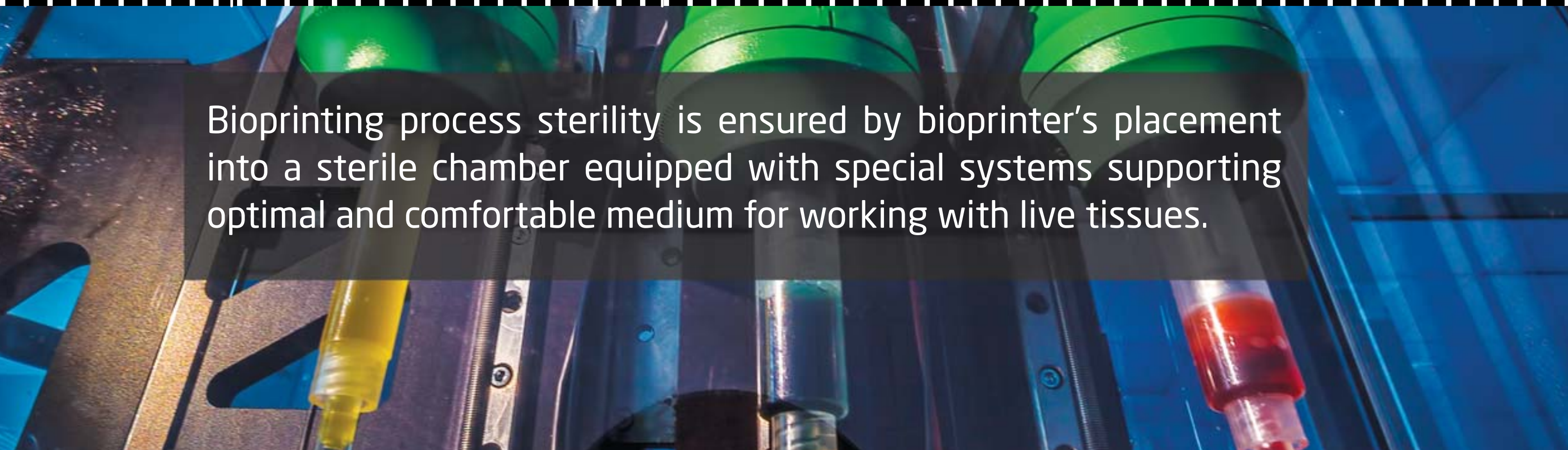
1. **Multifunctionality.** FABION bioprinter supports all known methods and techniques of 3D bioprinting.
2. **Unique system** of UV-induced hydrogel (biopaper) polymerization operates without contact with spheroids and cells thus avoiding any printed cells' DNA damage unlike most existing engineering solutions for hydrogel polymerization, which are used in some other commercially-rated bioprinters.
3. **Combinativity.** The possibility of combining various bioprinting methods, techniques and materials. A wide variety of bioprinting process parameters that can be controlled with the help of the system's software additionally contributes to the device's combinativity.
4. **Accuracy.** Bioprinter's resolution matches the highest ISO standards.
5. **X-Y-Z positioning system is designed as a closed-loop automatic control system** which allows to achieve bioprinter nozzle positioning within the accuracy of 5 mcm and, therefore, accurate reproduction of the programmed digital model.
6. **Portability.** The design of this bioprinter's printing system ensures sufficient space for nozzle accommodation.
7. **Control.** 3D bioprinting process is monitored in real-time mode with the help of a built-in digital camera.

December 2013 – While developing a proprietary bioink, the company mastered mass production of tissue spheroids using non-adhesive silicone micromolds. Bioink and biopaper fabrication techniques were mastered and standardized.

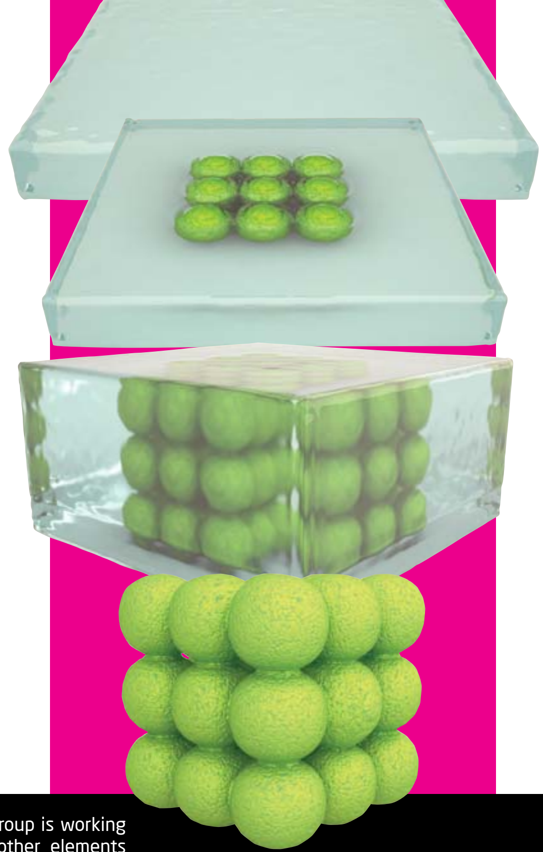
September 2013 – Research under way on 3D biofabrication of human organs under the approved conceptual plan and under the supervision of V.A. Mironov. (V.A. Mironov – tissue engineer, the inventor of the human organs 3D printing technology, M.D., Ph.D., Prof., 3D Technologies Division at CTI, Brazil; Department of Biomedical Engineering at the University of Virginia; the author of patented inventions: «Fabrication of Nanofiber Vascular Grafts,» «Apparatus for Tissue Spheroid Fabrication,» «Hydrogel for 3D Tissue Construct Fabrication,» etc.)

2014

January 2014 – *3D Bioprinting Solutions* bioengineering group proceeded with designing Russia's first bioprinter.



Bioprinter forms a layer of hydrogel (biopaper) onto which spheroids (bioink) are deposited as a next layer; layer formation is repeated a certain number of times as programmed and the layers formed in such a manner may differ. The process of layer formation continues until the final layer is printed. The method allows creating constructs with complex inner structure.



Tissue spheroids are cell aggregates. Spheroid's characteristics depend on the type of cells, which were used for its «fabrication.» For example, spheroids fabricated of endothelial cells may be luminized spheroids with gaps characteristic of vascular system, while spheroids fabricated of epithelial cells will have no gaps, etc. The tissue construct bioprinting technology presupposes using spheroids of different tissue origin, which allows assembling complex organic constructs.

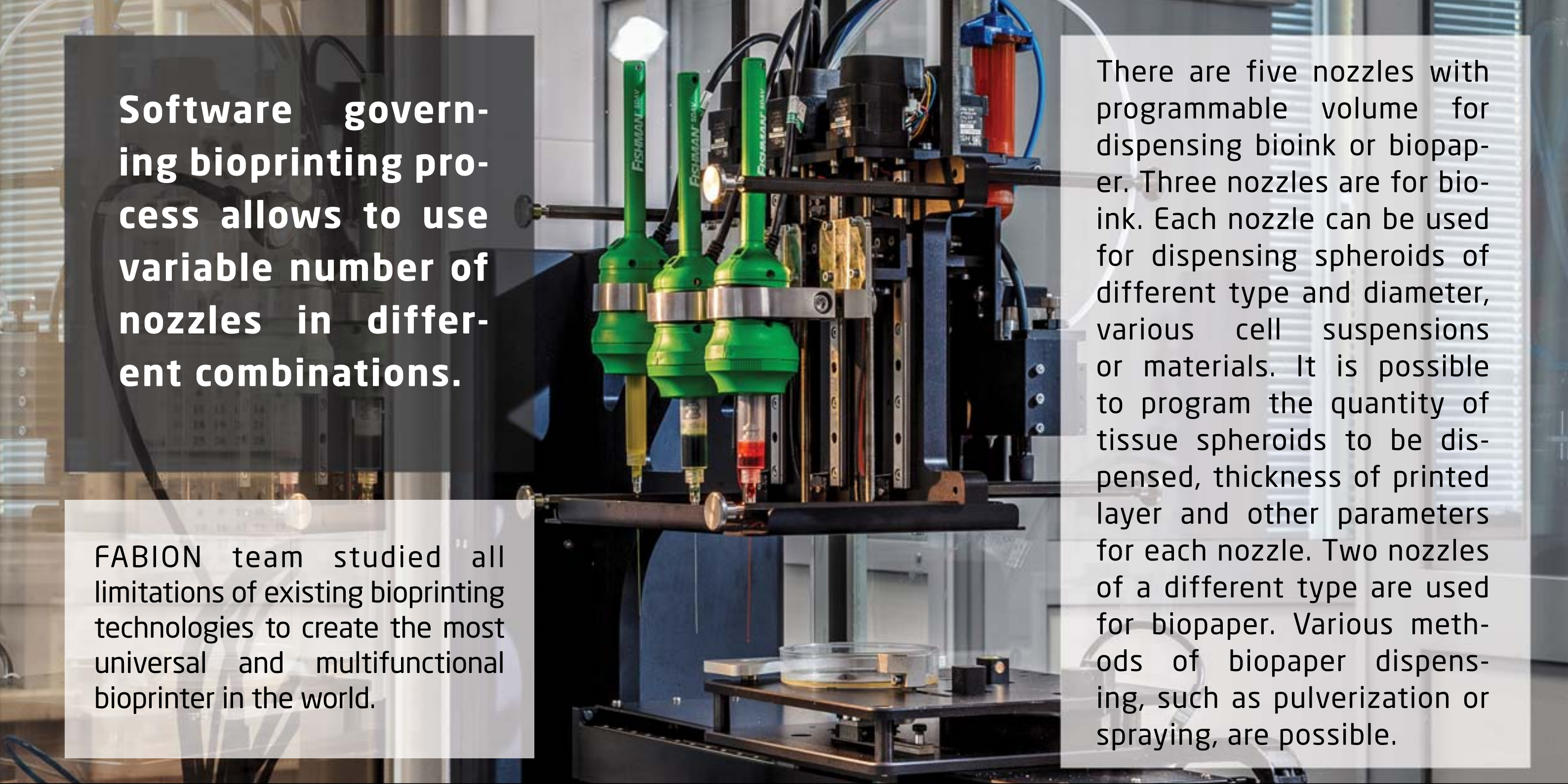
Biodegradable hydrogels are used as **biopaper.** The main functions of hydrogel include holding spheroids in certain preset locations in space and serving as nutritive medium for cells.

April 2, 2014 – the *Discovery of the Year* award for 3D Bioprinting Solutions.

May 2014 – *3D Bioprinting Solutions* was awarded an international registration certificate.

June 2014 – 3D Bioprinting Solutions Research Group is working on creating of a bioreactor, as well as some other elements of biofabrication technological platform, and a new bioprinter modification which unique selling point is purpose-built software.

Tissue spheroids or bioink is the key element of the 3D bioprinting technology – building blocks of which 3D tissues and organs are constructed. Tissues spheroids have many remarkable properties, however, the most important one for 3D printing is their intrinsic ability of «self-assembling» or «self-organization» in the process of tissue fusion governed by the force of surface tension, i.e. their ability to launch tissue fusion process. The natural phenomenon of tissue spheroid fusion underlies robotic biofabrication of 3D tissue and organic structures using a bioprinter.



Software governing bioprinting process allows to use variable number of nozzles in different combinations.

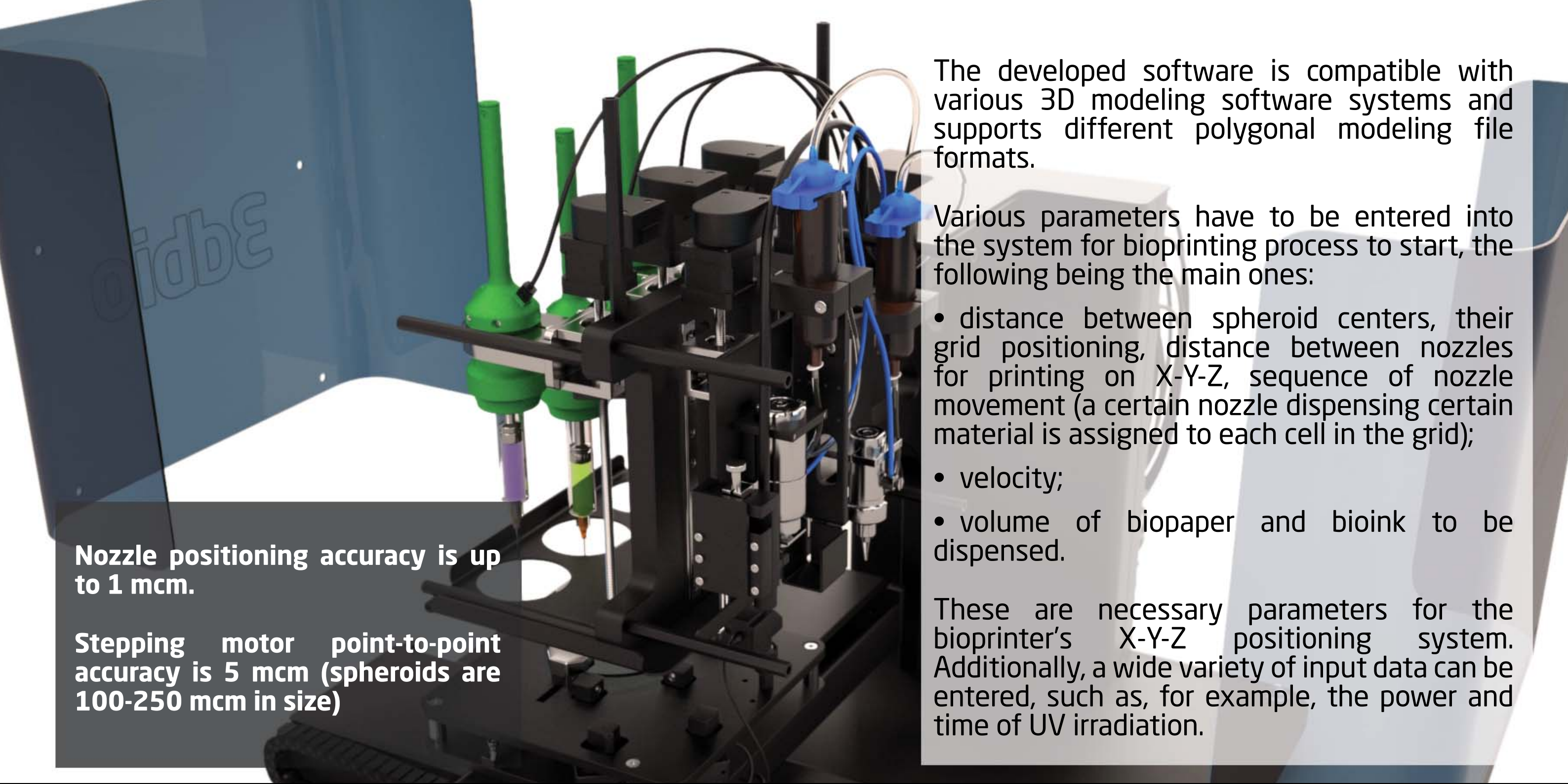
FABION team studied all limitations of existing bioprinting technologies to create the most universal and multifunctional bioprinter in the world.

There are five nozzles with programmable volume for dispensing bioink or biopaper. Three nozzles are for bioink. Each nozzle can be used for dispensing spheroids of different type and diameter, various cell suspensions or materials. It is possible to program the quantity of tissue spheroids to be dispensed, thickness of printed layer and other parameters for each nozzle. Two nozzles of a different type are used for biopaper. Various methods of biopaper dispensing, such as pulverization or spraying, are possible.

- September 2014 — 3D Bioprinting Solutions laboratory presented Russia's first bioprinter of original design and make. Work goes on to optimize bioprinting process, develop different types of bioink and biopaper with different properties, further perfect the technology of 3D printing of biological constructs.
- October 2014 — Team started working to organize mass production of bioink using microfluidics, which allows forming more than 1,000 spheroids per second is in progress.
- October 5, 2014 — Work on further perfection of bioreactor and other elements of biofabrication technology hardware.

Technology potential

Non-medical use of bioprinting includes creating 3D functional models of human tissues and organs for toxicological, pharmacological and radiological studies as well as for in vitro and in vivo modeling of human diseases. Bioprinting technology can become an innovative, environmentally-friendly and humane method of commercial scale production of meat, leathers and furs, radically different from the methods currently used in conventional agriculture and food industry.



The developed software is compatible with various 3D modeling software systems and supports different polygonal modeling file formats.

Various parameters have to be entered into the system for bioprinting process to start, the following being the main ones:

- distance between spheroid centers, their grid positioning, distance between nozzles for printing on X-Y-Z, sequence of nozzle movement (a certain nozzle dispensing certain material is assigned to each cell in the grid);
- velocity;
- volume of biopaper and bioink to be dispensed.

These are necessary parameters for the bioprinter's X-Y-Z positioning system. Additionally, a wide variety of input data can be entered, such as, for example, the power and time of UV irradiation.

Nozzle positioning accuracy is up to 1 mcm.

Stepping motor point-to-point accuracy is 5 mcm (spheroids are 100-250 mcm in size)

October 21-22, 2014 — Russia's first international conference on 3D bioprinting and biofabrication by *3D Bioprinting Solutions* Laboratory in cooperation with the Skolkovo Innovation Center and I.M. Sechenov First Moscow State Medical University.

2015

March-April 2015 — Bioprinting of thyroid gland, research to create a live functional organ.

Late 2015-mid 2016 — Task is set by the laboratory's chief of research to develop a first clinical in vivo biopinter — *biopen.*

2016

Hypergoal is to «fabricate» by means of bioprinting such complex organs as kidneys.

3D bioprinting technologies are currently developed in the following countries: The U.S., Switzerland, Australia, Canada, UK, Singapore, China, Germany, the Netherlands, France and Japan. In Russia, *3D Bioprinting Solutions* manufactured Russia's first bioprinter.

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