Cell culture support for controlled ultrasonic stimulation

INVENTORS: Leonardo Ricotti,
Andrea Cafarelli,
Francesco Fontana,
Tiziano Pratellesi

CO-OWNER: BAC Technology

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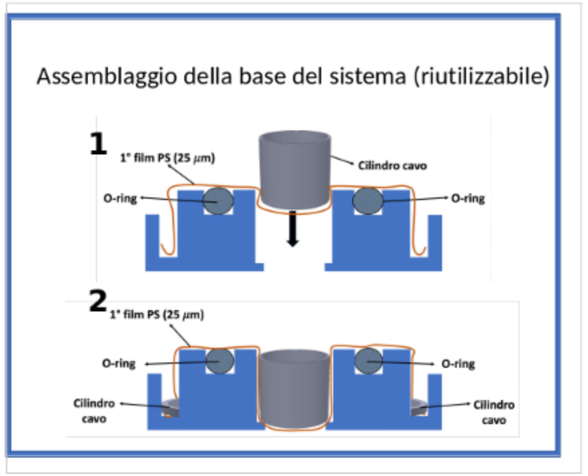
Invention

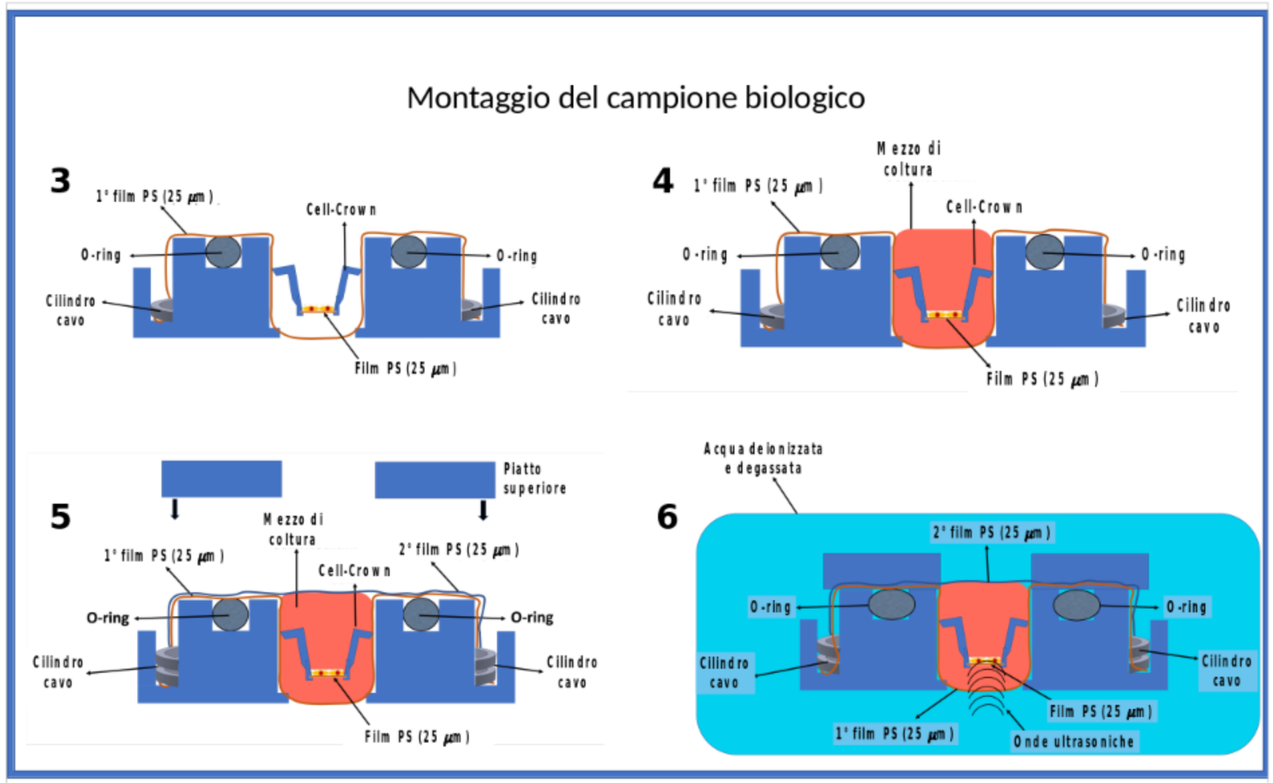
Low intensity pulsed ultrasound (LIPUS) is a specific category of ultrasound currently used to accelerate tissue regeneration and to treat bone fractures, chronic wounds and venous ulcers, as well as injuries to tendons, cartilage and other tissues. Other applications, such as inhibition of the inflammatory response and neuromodulation, have also been recently investigated. However, even if various therapeutic applications of LIPUS have been demonstrated at a preclinical and clinical level, the mechanism underlying the interaction between ultrasounds and cells, between ultrasounds and tissues, as well as between ultrasounds and materials in general has not yet been fully understood. Scientific research is carried out, both in vitro and in vivo, with the aim of penetrating more deeply into the understanding of the correlation between the cause (ultrasonic stimulation) and the effect (material or cell / tissue response). A major problem hindering further progress in ultrasound-based therapies is the often inaccurate measurement and poor control of ultrasound exposure conditions. This aspect is crucial for identifying a reliable correlation between the ultrasonic dose administered and the effect observed on cells or materials. Many researchers in this field exploit ultrasound using non-standard configurations, both in in vitro and in vivo conditions. Therefore, many experiments are susceptible to errors both during the calibration phase and during use. In particular, it is known that in vitro tests are typically affected by errors in the actual ultrasonic doses administered to the targets, up to 700% of the expected values. This occurs due to various physical phenomena, such as attenuation, reflection, refraction, generation of standing waves and the like. The results available in the state of the art, while leading to positive results in some cases, are difficult to compare, slowing the progress of this type of technology. Any attempt to determine a quantitative relationship between ultrasonic exposure and the observed effect, in fact, should be based on reliable measurements of the ultrasonic field that is applied, as well as on an appropriate design of the test bench. In the wake of these considerations, the purpose of this invention is to provide a biological housing system capable of undergoing highly controlled ultrasonic stimulations, capable of guaranteeing, at the same time, practicality and simplicity of use, low cost and complete sterility. of the biological samples tested.

The solution must meet four basic requirements:

1. It must guarantee complete transparency to the ultrasonic waves (i.e. prevent unwanted reflections and attenuations, so as to be able to control the dose).
2. It must ensure the sterility of the samples under stimulation with respect to the external environment, and therefore, being the stimulations conducted in degassed and deionized water, their impermeability. practicality and simplicity of use: the system must be characterized by several culture chambers. By creating more chambers, in fact, it is possible to stimulate more biological replicates at the same time (obviously using more ultrasonic transducers), optimizing the times.
3. Furthermore, it must be assembled, disassembled and used quickly and easily.
4. low cost: the system must not consist of completely "disposable" elements, but of a reusable base, minimizing the disposable component, and therefore minimizing the costs of use. The proposed solution uses a polystyrene film (Goodfellow, Huntington, Cambridge, UK) able to guarantee transparency to ultrasonic waves: the film has a thickness of 25 □m, which is much lower than the minimum wavelengths typically used for ultrasonic high frequency stimulation (300 □m at 5 MHz) . In this way, therefore, the phenomena of physical attenuation are minimized. The transmission values of the ultrasonic wave through the film were experimentally identified as the frequency used varied, obtaining the following values (Table 1):

Drawing & pictures





Industrial applications

- Improve theunderstanding of the correlation between ultrasonic stimulation and material or cell / tissue response.
- Potential new treatments for bone fractures, chronic wounds and venous ulcers, as well as injuries to tendons, cartilage and other tissues. Other applications, such as inhibition of the inflammatory response and neuromodulation, can also derive from this invention

Possible developments

The research group is open for discussions with industrial partners interested in licensing the technology covered by this patent.

For more information:

Scuola Superiore Sant'Anna – Technology Transfer Office

Headquarters: Piazza Martiri della Libertà 33, 56127, Pisa

Web site: www.santannapisa.it

E-mail:uvr@santannapisa.it

For more information:

Ufficio Regionale di Trasferimento Tecnologico

Headquarters: Via Luigi Carlo Farini, 8 50121 Firenze (FI)

E-mail: urtt@regione.toscana.it

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