Introductory Course **Medical Applications for Micromachines Part 2**

From Macro to Micro

From the beginning of the development of micromachine technologies-now proceeding for over ten years-it has been considered that the field of medical care held the potential for the most important, and furthermore, most basic demands. This time also saw the start of the transfer of practical technologies from the macro world to the micro world-or in other words, to the submicroscopic world-with the field of medical care being represented in the form of micro surgery. The principal reason for this lay in the fact that medical care had become focused on treatment; furthermore, this in turn resulted from the dimensional change which occurred in the field of medical care over the past ten-odd years: Specifically, treatment began to move away from classical, macro applications such as the removal of unneeded organs or, for example, the injection of medicines over the entire body, and it started to develop in a world where cells, tissue, or even organs which were less than a centimeter in size or even smaller became the primary subjects for application. Cells are the primary elements of life; accordingly, a realization developed that as the subject for application of medical technologies became smaller and smaller, it would become possible to conduct medical activities which would be more significant in terms of human life. In addition, it also became possible for several medical technologies from the micro world to be put to developmental use.

In the case, for example, of surgical practices-as represented by micro surgery-over fifty percent of all related fields now involve actions requiring a loupe or microscope; furthermore, micro-forceps and micro-scalpels have now been applied to use for these tasks. Even in the case of the endoscope operations which have revolutionized the world of surgery over the last ten years, these have become characterized by micro-remote operations carried out via a trocar of less than one centimeter in diameter. Originating from manual industrial methods, these operations have begun to change in a fundamental way through the incorporation of rapidly-developing video-data technologies and also through the implementation of technologies from the world of artificial-reality sensing. Already, a large portion of the scalpels, syringes, and micro catheters which are used for the purpose of actual in-body operations in the microscopic realm are provided as one-application, throwaway devices, and for this reason, the majority of the associated technologies now require mass-production processes which employ industrial technologies. It may be said, therefore, that the world of micromachine technologies has now for the first time developed a need for industrial operations.

From Micro to Nano

Occurring almost simultaneous with the start of transition from macro to micro for those items subjected to medical-treatment practices, the subjects of examinations also began to switch from microscopic cells and metabolites of a certain density towards cell-internal organelles, genes, and minute volumes of immune-system substances; similarly, such examinations have also begun to deal with items and substances which are more important with regard to life control. Since the dimensions of cell-internal substances now correspond to the nano level, and because it is now necessary to handle extremely low densities measured in nanomoles, it may be said that a shift from micro to nano is beginning to occur for examination items. We cannot allow ourselves to ignore the passage over the past ten-odd years-as characterized by the human genome project and the like-of the science of biomedicine into the realm of the nanometer.

Although the development of biomedical examination elements and devices has been overlooked during the course of previous micromachine projects, it may be taken for granted that bio-elements, chips, and the like will be incorporated into the next generation of micromachine and nanomachine technologies Furthermore the last few years have seen rapid development both in the field of industrially-manufactured DNA chips, protein immunochips, and the like, and also in the field of micro-inspection elements as typified by on-chip labs which are put to bed-side use as liquid inspection chips; these developments, too, may be considered as a natural matter of course. As indicated by the announcement of the DNA chip in 1997, the development of post-genome technologies in the field of biomedicine is being

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carried out with its aim set squarely on the nano world; furthermore, bioindustry has begun creating a huge industrial base for the twenty-first century. Naturally, medical technologies have also started to directly handle items such as tissue and cells, and deserving of particular attention is the commencement of studies within the field of genetic medicine focused on intracell injection methods for substances with dimensions between several microns and severalhundred nanometers. These studies have been started due to the meaningful medical treatments for a wide range of sicknesses which will be possible if remote operations can be used to inject a specific DNA probe into a target cell. The Arrival of Nano Quantum Systems

Suitable handling technologies will be required in order that substances and items of nano-dimensions may be directly operated on, and the majority of these correspond to micromachine technologies. In this world, however, problems lie hidden in the nano region-the region where micromachines now reside. The DNA base pairs as used by biochips are of several nanometers in dimension, and on-chip labs handle material volumes which are less than a nanomole (i.e., 10⁻⁹) in concentration. As indicated recently by many researchers, the reduction of dimensions which accompanies the shift toward micromachine technologies has, when considered from the point of view of material units, reached the realm of several molecules, and further reduction to the quantum level cannot be avoided. The materials which are subjected to direct operation in the majority of medical-chemistry examinations have material volumes of the nanomole level. Since a solution containing 6×10^{23} molecules per liter is said to have a concentration of one mole, one cubic millimeter of a one nanomole solution will contain 6×10^5 molecules. Accordingly, in the world of nanomole examinations where elements of ten microns in size are used, an examination chamber containing one nanomole of solution will actually hold a $1/10^6$ fraction of this number-in other words, 0.6 molecules. Micro-TAS (total analysis system) and other similar technologies recently under development have incorporated this dynamic, open-system world; accordingly, this indicates entry into the realm of quantum-wave mechanics, where physical laws become uncertain with regard to classical and deterministic theories

Meanwhile, in the case of micromachining technologies where the one-micron barrier has already been broken, the size of the examination elements which this creates has dropped to a level measured in cubic-micron units. In micromachines which have been manufactured with dimensions close to one micron, the majority of macro-world rules will not be applicable with respect to induction of the chemical reactions which handle the substances contained. Analysis in the micromole range has recently become the most commonly-applied, and with the exception of those cases which handle protein structures and other substances of a certain degree of size, it may be said that for this type of analysis also, a solution must be found for the electronic-related uncertainty problems in systems which perform analysis using commonlyapplied electrochemical electronic reactions. If nanomoles are to become the subject of operations, this world will expand to include technology where today's regularly-produced micromachines have sides of one-hundred microns, and it is quite possible that new technologies will be required for examination and materialidentification purposes. In other words, if the world of micro electromechanical systems were to coincide with the world of organisms containing aqueous solutions, this would lead to the start of the creation of, not a micro world, but a nano world; furthermore, it should be emphasized that biomedical micromachines have already entered the realm of the nano machine, and that further reduction to the level of nano-quantum systems is an inevitability.