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Frontier**

by

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Maintaining a state of physical well-being is highly important to us, so perhaps it is no surprise that medicine and medical technologies have persisted nearly as long as we have. Medical technologies have evolved greatly since our ancestral past. Today, the vast array of current medical technologies, from the CAT scan to the pacemaker, has magnified the scope and power of medicine in our lives. To those with access to these technologies, the length of life has increased and the overall state of health has improved dramatically. Medicine of the future, however, will perhaps be even safer, more efficient, and ultimately more powerful than it is today because doctors will utilize the power and practicability of microscopic tools and devices – invisible to the naked eye but potent enough to combat disease. Although miniaturized medical technologies will revolutionize the way we treat disease and physical suffering, it will be important as scientists and engineers continue to develop these powerful new technologies that understand the potential they hold for both good and ill.

Technologies existing or functioning at the molecular level – collectively referred to as nanotechnology – have been largely speculative in terms of how they will change the nature of healing, since they have not yet been applied to modern medicine. Development of nanotechnology has only existed since the latter part of the 20th century, and scientists are just now beginning to create and manipulate simple structures at the atomic and molecular levels. In theory, this application of nanotechnology to medicine is referred to as nanomedicine, and involves the implementation of technologies that exist or function at the cellular and sub-cellular levels, for medical use. In the words of scientist Robert Frietas, nanomedicine will involve the “designing and building...of incredibly efficacious

molecular devices, and then deploying these devices in patients to establish and maintain a continuous state of human healthiness” (Frietas 16-17). The prefix “nano” as it is used here refers to one-billionth; thus, nanomedicine refers to technologies on the scale of a billionth of a meter (24). To put this in perspective, imagine this letter *e*. This letter is about 1 millimeter wide. Now shrink this 100,000 to one million times and you will reach the approximate width of a nanodevice. The typical human hair has a width of about 10,000 nanometers.

The original concept for sub-microscopic technologies came in the late 1950’s, the brainchild of the late physicist Richard P. Feynman. Dubbed “the father of nanotechnology” by fellow scientists, Feynman expounded on the future of miniaturization, and set the stage for future scientists to begin exploring the creation of molecular-sized machines. In 1959, Feynman delivered a speech entitled “There’s Plenty of Room at the Bottom” at the American Physical Society that opened the doors to research into the fabrication of nanotechnology. “The principles of physics, as far as I can see, do not speak against the possibility of maneuvering things atom by atom,” he said. “[I]t would be, in principle, possible...for a physicist to synthesize any chemical substance that the chemist writes down.... The problems of chemistry and biology can be greatly helped if our ability to see what we are doing, and to do things on an atomic level, is ultimately developed” (Feynman).

Four decades later, nanotechnology has now proven itself to be a viable, and potentially powerful, engine of change – especially in the field of medicine. New fabrication strategies have been developed to create electronic and mechanical components on an ever-decreasing scale. Currently, there are several primary production methods termed “top-down,” which involve lithographic procedures, and the “bottom-up” method. One top-down method entails a modification of conventional photolithographic procedures. Photolithography, used to manufacture computer chips and microelectronic systems, can be used to create nanostructures by designing a circuitry pattern on a metallic film, and subsequently transferring it to the surface of a silicon wafer (Whitesides and Love 40).

Similar methods involving lithography include what is termed “soft lithography” and scanning probe methods. Soft lithography is typically carried out by making a mold or stamp on a silicon wafer, using photo- or electron-beam lithography to create a pattern on the stamp. The stamp then “reproduces features from the master as small as a few nanometers” (Whitesides and Love 43). Scanning probe methods involve the use of powerful tools such as scanning tunneling microscopes (STM’s) or atomic force microscopes (AFM’s) to move individual molecules and arrange them in patterns (45). In either case, tiny probes on the AFM or STM release organic molecules from their tips, which bond to a special metallic writing surface. Using hundreds of parallel probes in concert could lead to rapid manufacturing of complex structures on the molecular level (Rotman 64).

A second manufacturing strategy involves what is termed “bottom-up” – that is, starting at the molecular level and building nanostructures from these molecular building blocks. Bottom-up entails literally “growing” nano-sized crystals, some as small as several nanometers across. Bottom-up methods generally result in the creation of simple particles instead of complicated, interconnected patterns. Using bottom-up technologies, structures such as nanotubes and quantum dots (also known as semiconductor nanocrystals) can easily be fabricated (Whitesides & Love 45).

So why create devices so small in the first place? Manufacturing nanoscopic medical devices or components for larger devices would have several significant advantages in the medical field. Being able to manipulate matter on the most fundamental biochemical level – the molecular level – would mean gaining control over the building blocks of larger biological substances. In our bodies, for instance, most of the activity that occurs on a daily basis takes place at the cellular and sub-cellular levels. Affirms Robert Frietas Jr., author of *Nanomedicine*, “Human health is fundamentally biological, and biology is fundamentally molecular” (16). The biochemistry responsible for the functioning of our bodies occurs well beyond what we can see with the naked eye. Devices small enough to work at this level would undoubtedly be a boon to physicians, because problems could be addressed directly at the biochemical level. Fiedler and Reynolds insist that

nanotechnology will “permit on a programmable basis exact control of molecular structures that are not readily manipulable by organic means” (597).

Molecular devices would mean future access to parts of the body that are currently inaccessible using larger and clumsier technical equipment, or that are accessible only through invasive surgical procedures (Frietas 27). Imagine a machine that could travel through the bloodstream and repair damaged tissue and organs without requiring a surgeon to physically break the surface of a patient’s skin. A device such as this might spell the end to the kind of invasive surgery we are accustomed to today.

Furthermore, medical devices employing the use of nanostructures could allow drugs and other therapeutic agents to target specific areas of the body. At MIT, for example, research scientist Robert Langer is working on an implantable chip that could act as an individualized pharmacy, delivering medication directly to diseased areas of the body (Thieme 28-29). Site-specific therapy is of great importance in health care; technologies with this ability could save thousands of lives each year that would typically fall victim to drug reactions. According to Leon Jaroff, as many as 100,000 deaths result each year from harmful drug reactions (Jaroff par1). Site-specific therapies would also reduce the severity of many side effects, such as those from chemo- or radiation-therapy for cancer patients (Freitas Jr. 34-35). Administering conventional chemotherapy to destroy brain tumors has been difficult because of the non-porous nature of the blood-vessel walls in the brain (Jaroff par10). Drug-bearing wafers implanted at the site of the tumor could slowly release a tumor-fighting drug. A clinical trial in 1997 using this technique showed promising results (par10). Targeted implants would also be much more efficient than pills, since pill often break down in the digestive system before they even reach the bloodstream (Thieme 28).

Technologies like the pharmacy chip would have many other benefits besides those due to site-specificity. Firstly, programmable implanted chips would likely be safer than pills or injections, which can cause dangerous fluctuations of drug concentrations. Sensors and microprocessors on board implanted chips could alter the timing or quantity of dosages to meet the individual’s needs. Furthermore, chips might lead to simpler medical attention,

asserts Trevor Thieme, author of “A Pill with Your Name on It.” Physicians might be able to simply “download a patient’s blood biochemistry readings on demand via a wireless link, evaluate the response to medication, and adjust the treatment by remote control” (28).

In addition to pharmaceutical microchips, some scientists are working to develop miniaturized biosensors that would work in conjunction with implanted “pharmacies.” These sensors would enable drug-stocked chips to respond to alterations in the body’s biochemistry. According to Alexandra Strikeman, author of “The Programmable Pill,” a biosensor of this kind could “sense when concentrations of a drug were too high or too low...and tell the device to respond accordingly” (83). IBM scientist Christoph Gerber believes that biosensors utilizing nanotechnology might also prove to be a simple way of detecting specific proteins in the body. Gerber suggests the possibility of future implanted microcapsules for drug delivery that have a nanoscale valve able to detect signature proteins from cancer cells, for example (Rotman 66). On a broader scope, the use of increasingly smaller devices means faster and more precise diagnoses. The continual quest for smaller, faster processing and storage chips has allowed for faster processing of information and more storage of data in smaller volumes of space. Robert Freitas, Jr. asserts that “the analytic function of medical diagnosis requires rapid communication between the [delivered] devices and attending physician...Nanomachines [will be able to] outmessage the results of in vivo reconnaissance or testing literally in seconds” (34). Mechanical nanoinstruments will be able to run a greater number of diagnostic tests of greater variety in less time than current measures. Furthermore, believes Freitas, nanoscopic devices such as nanorobots will one day be able to “report back to the attending physician...a summary of diagnostically or therapeutically-relevant data describing exactly what was found...and what problem were encountered, in every cell visited” (34).

Perhaps some of the greatest benefits will come from the use of nanorobots and similar miniaturized devices. At Cornell University, researchers have already developed the prototype of a bionic nanomachine, composed of an enzyme molecule coupled to a

metallic substrate. Devices such as these could perhaps be designed to hunt down and destroy invading pathogens or malignant cells, or used in drug therapy (Segelken par1,3). James Baker, chief of the allergy and immunology department at the University of Michigan's Medical School, and founder of the University of Michigan's Center for Biologic Nanotechnology, believes that nano-sized synthetic molecules called dendrimers can be used to infiltrate living cells and detect pre-malignant and cancerous changes. These dendrimers could then destroy any threatening substance or cells with powerful chemical agents (Voss par 21).

Michael Singletary of the University of San Diego has also theorized using nanotechnology in the fight against AIDS. Current AIDS drugs, he claims, have dramatically slowed the growth and spread of the virus, but none have currently been able to attack the virus directly (par 1). Singletary has suggested engineering a device that can attach to the "head" of an HIV molecule that will induce other parts of the immune system into action that don't require the use of T-4 cells (which are destroyed by the invading HIV molecules) (par 2).

Nanobots, if viable, could be used for myriad other medical purposes, such as removing arteriosclerotic deposits, repairing cellular damage, or possibly, as futurist K. Eric Drexler believes, providing doctors with a superior means of anaesthetizing a patient (111-112). Even more significantly, however, cellular repair machines might pose a solution to the aging problem. The deterioration of the body that comes with aging makes it susceptible to a host of other diseases and eventually leads to death. If aging is the result of a few regulatory processes, according to Drexler, than nanomachines many provide a solution by being able to reverse the natural processes of biostasis and repair or restructure dying or damaged cells, allowing us to live longer and healthier lives (114-115).

The great panoply of medical benefits that nanotechnology will potentially offer seems almost too good to be true. There are some concerns, however, about the social and ethical implications associated with nanomedicine. The inherent power over cell and

molecular manipulation that nanotechnology will provide inevitably leads to questions about its potential for ill. One concern is that molecular-based medical technologies will lead to problems with overpopulation by extending the length of lives across the globe (Drexler 124). Currently, some parts of the world are already experiencing the effects of overpopulation. Already, modern medicine has saved millions of lives and extended the length of life longer for many, nanomedicine promises to treat almost any kind of disease and possibly suspend the onset of death. Extending the length of life and eradicating diseases will undoubtedly lead to conflict between the growing number of human beings and the finite number of resources. As bioethicist John Harris has observed, although the prospect of personal extended life-span is likely to be widely embraced, “it is one thing to contemplate our own “immortality,” quite another to contemplate a world in which increasing numbers of people live indefinitely, and in which future children have to compete with previous generations for jobs, space, and everything else” (par 5).

Any technology that has the power to tamper with the basic elements of our humanity opens an ethical can of worms. Genetic engineering has already unleashed a whirlwind of controversy. Nanotechnology may very well produce a similar controversy, because it promises to manipulate the human body at the most fundamental level. Nanotechnology may eventually aid in genetic engineering through the manipulation and modification of DNA molecules (Hameroff 269). Nanotechnology may provide the means to live well beyond a hundred years, or augment our already existing faculties to obtain a “superhuman” state (Fiedler & Reynolds 621-622). Modifying our bodies to exceed our natural limitations could prove to have far-reaching, and many unintended, consequences. Undoubtedly, our own perceptions of mortality would change if such precedents were made. In an article by Richard H. Smith, entitled “Social, Ethical, and Legal Implications of Nanotechnology,” the author contemplates whether sophisticated nanomedical capabilities in the future will change the way society looks at risky behaviors (209).

There are ethical risks and dilemmas also associated with the implantation of medical devices. Is it a violation of one’s privacy, for instance, to implant miniature communication devices that allow doctors to “see” what is occurring in a patient’s body

at all times? Nanosurgery might too allow for the control over an individual's genetic code. Is this safe for the patient? Does this give doctors too much control over an individual's biochemistry? Frederick A. Fiedler and Glenn H. Reynolds, in an article from the Southern California interdisciplinary Law Journal, point out that "nanosurgery has tremendous potential for alteration of people with resultant mixed results and subsequent opportunities for litigation...With such techniques available to them, unprincipled persons might have a field day" (620).

It has also been suggested that insurance companies will have an acute interest in medical progress concerning repair at any stage of illness. This is especially true for the early prevention of diseases that are chronic or expensive to treat (Fiedler and Reynolds 622). This raises the question of whether there will be discrimination on the part of insurance companies, and whether or not insurance companies will exert pressure on parents or physicians to correct these illnesses if easily and economically treatable (622).

Other difficult legal and safety issues would also arise with the use of such technologies. For example, if a nanorobot were to experience a flaw and malfunction, especially if replication becomes feasible, the result might resemble a virus, or worse (Fiedler & Reynolds 625). Who would be liable in such a case: the doctor or the engineer? What standards would be used to ascertain medical malpractice? How would such a problem be rectified? And assuming any treatment is safe, how would a treatment using a nanomedical device be classified: as a drug or a device? The distinction between a drug and device, as stated in the Federal Food, Drug, and Cosmetic Act, is not very satisfactory in the context of nanotechnology-based treatments (Fiedler & Reynolds 608).

Cost is another area of concern. Although it is assumed by many scientists, including Ralph Merkle and Eric Drexler, that the future of nanotech will herald mass production of nanodevices at inexpensive costs, production in the short-term may be very costly. According to Smith, "Fullerene-based computer chips may require enormously expensive fabrication facilities that turn out chips by the millions...This could result in a

proliferation of inexpensive unit costs but prohibitively (and anti-competitively) expensive initial capital costs” (Smith 209).

Undoubtedly, nanomedicine – and nanotechnology in general – is very new territory for mankind. The benefits to the health and welfare of humanity using nanomedicine seem great indeed, and I advocate the continuation of development of nanotechnology. However, as nanomedical and molecular-based technologies continue to evolve, I think it wise to refrain from blindly endorsing the implementation of such a catalytic force without first considering the possible risks and controversies that may arise. The past has shown us that new and promising technologies can often be difficult to control, especially if they are not fully understood. In an article entitled “Genetics and Human Malleability,” author W. French Anderson sums up this concern:

We may be like the young boy who loves to take things apart. He is bright enough to disassemble a watch, and maybe even bright enough to get it back together so that it works. But what if he tries to “improve” it?...The boy can understand what is visible, but he cannot understand the precise engineering calculations that determine exactly how strong each spring should be... Attempts on his part to improve the watch will probably only harm it...I fear...we, too, do not really understand what makes the [lives] we are tinkering with tick (452).

Looking with a retrospective eye to our experiences with biotechnology, we can hopefully locate certain areas of ethical concern pertaining to nanomedicine. Undoubtedly, as some scholars suggest, it would be useful to pursue questions that earlier technologies evoke (Weil 194). We must consider and deal appropriately with the risks involved. For these ends to met, it is critical that there is enough public interest and scientific responsibility to generate public discussions on the development and potential consequences of nanotechnologies. “Conversation between people in nano research and development and members of the public is necessary,” says Vivian Weil, director of the Center for the Study of Ethics in the Professions at the Illinois Institute of Technology. “People will have to learn to identify interests, their own and those of other parties to the

conversation” (195). Education will be fundamental in changing and developing ethical approaches to nanotech research (196-197).

It is said that hindsight is 20/20. Although biotechnology at the molecular scale reveals new moral, ethical, and legal quandaries, learning from our history with other technologies may hopefully allow us to eliminate, or at least mitigate, some of the potential problems of nanomedical technology. If we can do this, nanomedicine may prove to be a tremendous asset to humanity.

Bibliography

1. Alivisatos, A. Paul. “Less Is More in Medicine.” *Scientific American*. Sept. 2001: 67-73.
2. Anderson, W. French. “Genetics and Human Malleability.” *Intervention and Reflection*;
3. *Basic Issues in Medical Ethics*. Ed. Ronald Munson. 4th ed. Missouri: Wadsworth, 1992. 450-453.
4. Drexler, K. Eric. *Engines of Creation*. New York: Anchor Press, 1986.
5. Feynman, Richard P. “There’s Plenty of Room at the Bottom.” Lecture at the California Institute of Technology (1959). Zyvex. Jan 21, 2002.
<<http://www.zyvex.com/nanotech/feynman.html>.>
6. Fiedler, Frederick A., and Glenn H. Reynolds. “Legal Problems of Nanotechnology: An Overview.” *Southern California Interdisciplinary Law Journal*. 1994. Foresight Institute. 20 Dec. 2001. 594-629.
7. Frietas, Robert A., Jr. *Nanomedicine*. Vol 1. Austin: Landes Bioscience 1999. Foresight Institute. 1998-2001. Nov. 12, 2001.
<<http://www.foresight.org/Nanomedicine/>.>
8. Hameroff, Stuart R. *Ultimate Computing: Biomolecular Consciousness and NanoTechnology*. Amsterdam: Elsevier Science Publisher B. V. 1987. Ch10.
9. Harris, John. “Intimations of Immortality.” *Science Magazine*. Vol. 288. 7 Apr. 2000

10. Rotman, David. "Nanotech Goes to Work." Technology Review Jan/Feb 2001: 62-68.
11. Segelken, Roger. "Fantastic Voyage." 7 Sept 1999. Cornell University. 14 Dec. 2001.
<http://www.news.cornell.edu/releases/Sept99/bio_nano_mechanical.hrs.html.>
12. Singletary, Michael. "Medical Applications of Nanotechnology: Nanobodies." Abstract for a presentation given at the Sixth Foresight Conference on Molecular Nanotechnology. Dec. 12, 2001.
13. Smith, Richard H. "Social, Ethical, and Legal Implications of Nanotechnology." Societal Implications of Nanoscience and Nanotechnology (Report: March 2001). National Science Foundation. 16 Dec 2001. Section 6.5; 203-215.
<<http://itri.loyola.edu/nano/NSET.Societal.Implications/>.>
14. Strikeman, Alexandra. "The Programmable Pill." Technology Review. May 2001:78-83.
15. Voss, David. "Nanomedicine Nears the Clinic." Technology Review. Jan/Feb 2000. Nov 8, 2001. <www.techreview.com/magazine/jan00/voss.asp.>
16. Weil, Vivian. "Ethical Issues in Nanotechnology." Societal Implications of Nanoscience and Nanotechnology (Report: March 2001). National Science Foundation. 16 Dec 2001. Section 6.5; 193-198.
<<http://itri.loyola.edu/nano/NSET.Societal.Implications/>.>
17. Whitesides, George C., and J. Christopher Love. "The Art of Building Small." Scientific American. Sept 2001: 39-47.