Death, Brain Death, and the Death of Death:

Death as a Concept in Continuing Evolution

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NOTE: THIS ESSAY USES THE VANCOUVER (MEDICAL) REFERENCE STYLE

“It remains for the doctor and especially the anaesthesiologist, to give a clear and precise definition of "death" and the "moment of death" of a patient who passes away in a state of unconsciousness."   Pope Pius XII.

"Not only is she really dead, she's really most sincerely dead."
Munchkin Coroner in the Wizard of Oz, after examining the Wicked Witch of the East

Traditionally, death has been defined as the permanent cessation of the heartbeat and respiration. Modern developments in clinical resuscitation, however, have forced a reappraisal of this concept. Today, in hospitals around the world, ventilators, dialysis equipment and drug infusions that sustain the circulation often permit the bodies of critically ill patients to be artificially supported despite severe physiological insults, including death of the brain itself. In addition, the advent of transplantation surgery has provided a strong clinical motivation to allow death to be defined in terms of loss of brain function (brain death) or in terms of a relatively brief period of asystole (cessation of cardiac activity) in some patients (non-heart-beating donors). Finally, some thinkers argue that future developments in cryonics and nanotechnology may require further reappraisal of when a person is really dead. These issues are the subject of this essay, which presents as its central theme the notion that the concept of death is not static but rather is in a process of ongoing evolution.

The Traditional Concept of Death

Wikipedia defines death as “the permanent termination of the biological functions that define a living organism.” To clinicians, however, death has been traditionally been defined more simply as the permanent cessation of the heartbeat and respiration. Although this determination is usually not difficult to make, mistakes occasionally occur. For example, in Victorian times there were stories of individuals mistakenly being declared dead and later 'returning to life' when embalming began. (See, for instance, Edgar Allen Poe’s horror story "The Premature Burial", published in 1844, as well as Antoine Wiertz’s 1854 painting produced in homage to Poe’s story - shown in Figure 1.) In fact, the fear of being buried alive in Victorian times was so prevalent that some individuals requested that following their apparent death that they be buried in a coffin with an external bell mechanism that they could operate from inside their coffin should they regain consciousness while buried (Figure 2).

Figure 1

L'inhumation précipitée. Antoine Wiertz's 1854 painting produced in homage to Poe's story about being buried alive.

Image credit:

http://www.bc.edu/bc_org/avp/cas/fnart/art/19th/belgian/wiertz_burial.jpg

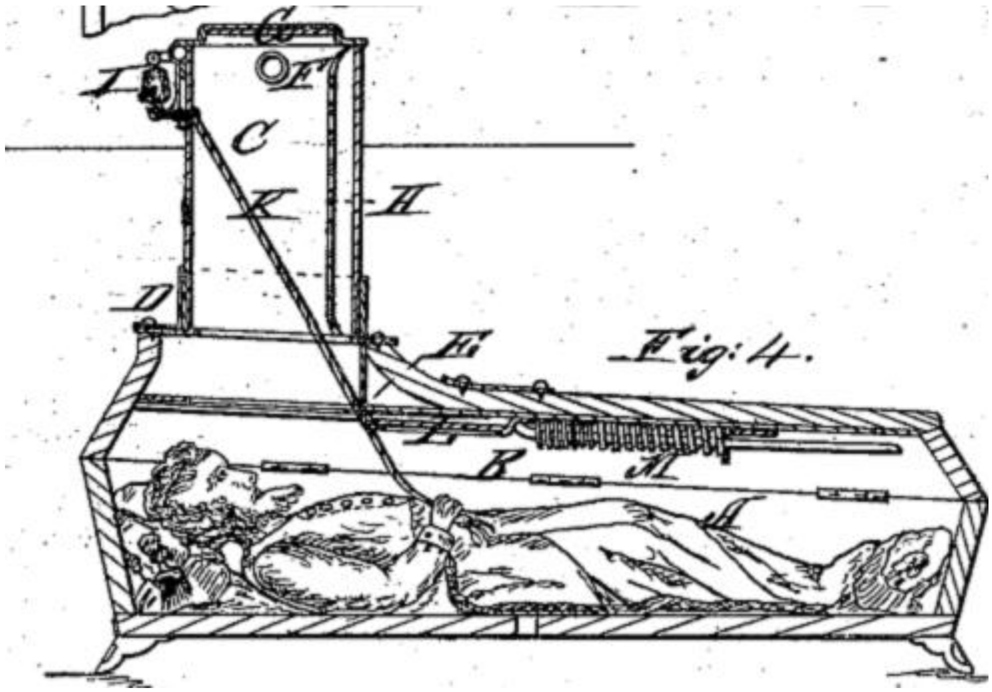

Figure 2

Figure from U.S. Patent No. 81,437 illustrating a mechanism where individuals who regain consciousness while buried can ring an external bell to signal for help.

Image Credit:

http://danfingerman.com/images/patents/0081437_4.gif

Brain Death

While the notion of death as permanent cardio-respiratory arrest has been familiar to physicians since biblical times, the notion of brain death is much more recent, having been developed in the 1960s as advances in transplantation medicine and medical technology provided a motivation to allow death to be defined in terms of loss of brain function [1]. This was because the success of transplantation surgery depends critically on the use of viable organs uncompromised by circulatory failure.

In a typical clinical scenario, a patient with a massive brain injury (for example, from a ruptured cerebral aneurysm) is treated in an intensive care unit. While there, the patient’s neurological status is periodically assessed and if there is suspicion that the patient is brain dead, a formal evaluation for possible brain death is carried out. If the patient is found to meet brain death criteria, the patient’s relatives are approached regarding possible organ donation. If they agree, cessation of life support measures are carried out after organ retrieval for transplantation has taken place. Cardiopulmonary collapse and classical death usually follows promptly [2].

The legal basis for brain death in the USA is the 1981 report of the President's Commission for the Study of Ethical Problems in Medicare and Biomedical and Behavioral Research [3]. The commission defined brain death as the "irreversible cessation of all functions of the entire brain, including the brain stem". Since that time this seminal report has been used as the basis for much of the discourse on brain death. Similarly, the World Medical Association has written that "It is essential to determine the irreversible cessation of all functions of the entire brain, including the brain stem" [4]. However, while these bodies have defined brain death in terms of "irreversible cessation of ALL functions of the ENTIRE brain," in the years since this definition has been widely adopted it has become very clear that many (perhaps most) patients diagnosed with brain death (and who have undergone organ harvesting) do not actually meet this requirement [5]. In particular, many patients diagnosed with brain death still have residual function in the hypothalamus, a part of the brain that contains a number of important nuclei, some linking the central nervous system to the endocrine system via the pituitary gland (hypophysis). Indeed, evaluation of hypothalamic function is not part of any brain death protocols in common use in the USA. Not surprisingly, inconsistencies of this kind are troubling to some clinicians, who would prefer that any possible logical inconsistencies in the declaration of brain death be avoided, no matter how small or clinically unimportant they may appear to be [6].

Similarly, some clinicians have noted that the criteria for brain death are in some respects a bit arbitrary. For instance, while the original Harvard criteria for brain death requires the loss of all spinal reflexes [7], more recent criteria do not [8]. Similarly, the various national guidelines are not all exactly identical, so it is likely that there are some patients who meet some existing national criteria for brain death yet do not meet others [9].

Issues such as these have lead to careful academic discussion in the medical literature, as well as to the airing of highly controversial television programs such as one from the BBC entitled: "Transplants: Are the Donors Really Dead?" [10,11]. Clearly, the concept of brain death can be said to be in evolution as these and other issues are discussed in various national and international forums.

Non-heart-beating Organ Donors

In more recent times, the lack of a sufficient number of organs from brain-dead donors has lead to the occasional use of non-heart-beating organ donors. Here, patients who are not brain-dead but have no reasonable chance of recovery are brought to the operating room where they are prepped for surgery, followed by the withdrawal of all life-support measures. Some time later their heart stops. A period of time later (typically 300 seconds after the final heart beat), surgeons quickly rush in to retrieve organs before they deteriorate [12].

Some individuals have criticized the definition of death used in non-heart-beating organ donation programs noting that any cessation of cardiac activity (asystole) might not necessarily be permanent as long the heart might be restored by vigorous resuscitation efforts [13]. In addition, several non-heart-beating organ donation protocols allow ante-mortem drug administration and other interventions that are not intended to benefit the donor. For instance, high-dose heparin is sometimes given to prevent blood clotting. However, since the heparin is not administered for the benefit of the patient, some professionals argue that its administration is unethical [14].

Another issue concerns timing. Doig and Rocker [14] explain the problem as follows:

> With the need to reduce warm ischemia, organs must be recovered as quickly as possible after the cessation of cardiac activity. The simple question becomes: when in the course of ascertaining death, is the patient dead, and when can organs be taken?

Referring to a report from the Institutes of Medicine [15] they also note:

> The recent Institutes of Medicine report identified variability between centres in the duration of asystole required prior to organ retrieval (2–20 min), and that limited research has been conducted on the likelihood of spontaneous “auto-resuscitation.” Their report recommended adoption of five minutes of observed cardiac asystole, with a caveat that further research is required to confirm that auto-resuscitation does not occur during this interval. Meanwhile, some centres

continue to use an interval of asystole as short as two minutes. Despite the premise of certainty in determining irreversible death, it is worrisome that centres can not agree to adopt a common standard.

Death as a Process (and not a Discrete Event)

In recent decades advanced studies into the biochemistry of physiological (apoptosis) and pathological (necrotic) cell death in mammalian organisms has led to new insights into the concept of death on the macro scale, i.e., the death of the entire biological organism. As a result of these insights, some individuals have advanced the philosophical position that organismal death is not an event so much as it is a process, and that life and death are not distinct binary states, but entities with degrees and gradations. Thus, while a patient may be legally declared to be dead a few minutes after the continued cessation of cardiac activity (as is done, for example, with non-heart-beating organ donation protocols), nevertheless, these individual argue, the cellular changes which occur in the period following cardiac arrest may be potentially reversible following the application of appropriate clinical interventions, especially under hypothermic conditions. (Indeed, if all cells and organs in an organism died fully and completely immediately following the last heartbeat, any retrieved organs would be completely unsuitable for transplantation.)

Based on such concepts, Bart Kosko, in his book *Fuzzy Thinking* [16], argues that we should think of "death in degrees" rather than death as a simple binary process. He suggests that the conceptual paradigm of "fuzzy logic", where membership in a particular class is taken as continuous rather than discrete, may be helpful in such a setting. An example may help explain this notion. A patient who has just had a surgical procedure may be asked to rate his or her pain between 0 (no pain at all) and 10 (worst pain imaginable). This pain score might be mapped into a pain "class" in some manner. For example, membership in the class "moderate pain" might take on 0% membership at a pain score of 4, and take on a 100% membership value with a pain score of 8. The class "severe pain" might be designed to start at 6 and take on 100% membership value at 10, the maximum possible pain score in the system. In the same vein, Kosko would have us talk about degrees of death, where one would have 100% death membership following cremation, but perhaps only 90% membership in the case of cryonic suspension (*vide infra*).

In a similar manner, the notion of "incomplete" brain death has now arisen in the medical literature [17], as might occur in the case of "the patient with a massive brain injury who meets the criteria for brain death only imperfectly, perhaps because one small patch of neurons in a brain-stem nucleus is still operating intermittently".

A number of thinkers are now speculating that future developments in nanotechnology may permit repair and rejuvenation of organ tissue that is either dead or nearly dead by classical criteria. When a cell is on a path towards death, for instance from oxygen deprivation, a number of complex biochemical events occur as energy is depleted from the cell. That is, under ordinary normothermic conditions, ongoing energy expenditure is needed to keep a cell alive. (The case is rather different under hypothermic conditions, as cellular metabolic rate decreases with decreased temperature. In fact some animals can even be frozen and later revived (e.g., wood frogs [*Rana sylvatica*]), presumably because of special components in the cells of these animals that prevent the formation of intracellular ice crystals that tend to destroy the complex internal machinery present in all cells.)

In his book *Citizen Cyborg* [18], James Hughes speculates that in the future clinicians may be able to launch nanobots (nanorobots) into patient’s bloodstreams and that these nanobots would be able to enter into cells just as viruses do today, and, just like today’s viruses, would be able to reconstruct internal cellular machinery. That is, just as an ordinary virus can alter cellular machinery to its own ends, it is hoped that nanobots designed along viral design principles might be developed that would conduct various kinds of cellular maintenance and repairs, such as: repairing damaged DNA, fixing leaks in membranes, repairing damaged ion pumps, etc. (Figures 3 and 4). Where such repairs are impractical or overwhelming, the nanobot might instead be used to trigger programmed cell death (apoptosis) to prevent the development of malignant cells that undergo uncontrolled growth. (Nanobots are featured in Michael Crichton's novel *Prey*, where a swarm of self-replicating nanobots capable of evolving new characteristics poses a threat to mankind.) Should these developments actually come to pass, it will require that we rethink our notions of death once again, since what was once irreversible damage would now be reversible.

Of course, not everyone takes such matters seriously. For instance, since cells contain thousands upon thousands of components that may be damaged, some authorities argue that developing the required nanobot for each conceivable type of cellular damage may be impossible, or at least highly impractical. Regardless, with such issues in mind, some thinkers have argued that it is helpful to distinguish between the definition of death based on cessation of the heart beat and a "more substantial" form of death, such as exists following cremation. In the later case, sometimes called "absolutely irreversible death" or "information-theoretic death" destruction of the brain has occurred to such an extreme any information it may have ever held is irrevocably lost for all eternity. This, some people argue, is the only real (irreversible) form of death.

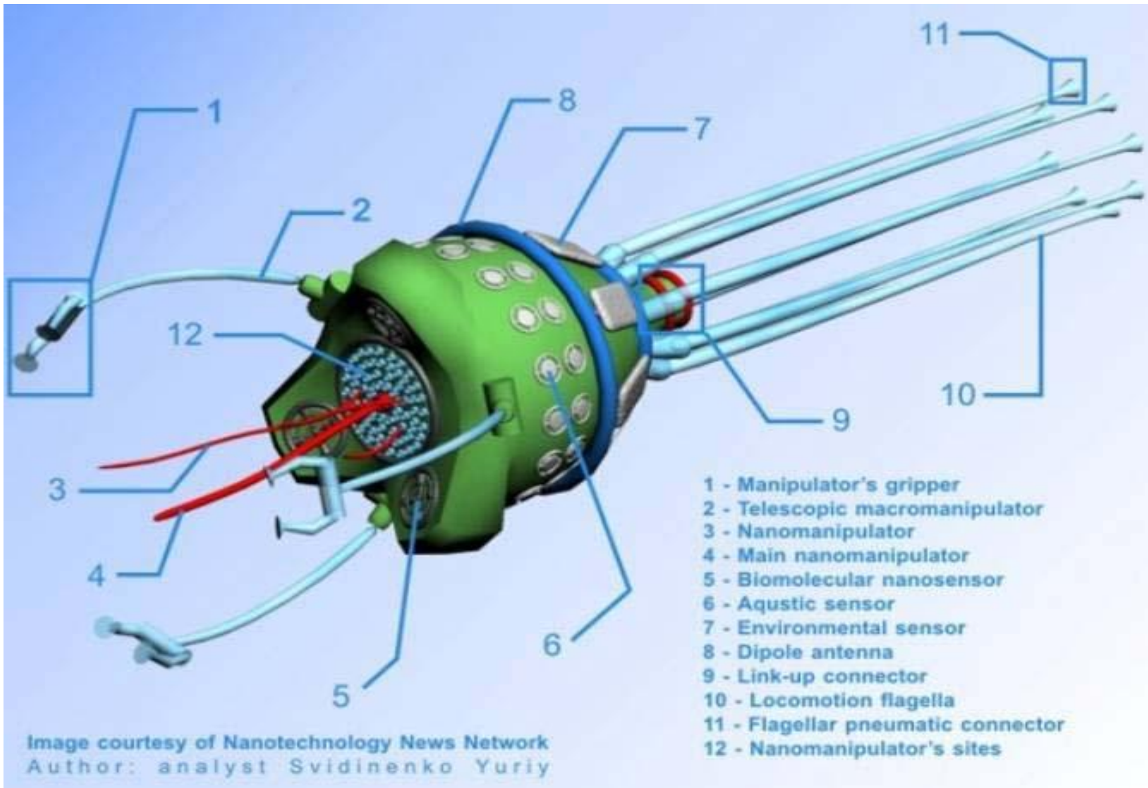

Figure 3: This artist's conception (schematic diagram) of a simple mobile cell-repairer diamondoid nanorobot with dimensions 1 x 1 x 3 microns (excluding flagella) includes mobility, a powerful bloodstream navigation system employing a wide range of sensors with fast molecular and cell identification, the ability to transport key molecules to and from internal storage systems, a broadcasting system to communicate with other nanorobots and with external macroscale computers, and long telescoping manipulators to grasp cells or other surfaces. Image and legend from http://www.foresight.org/Nanomedicine/Gallery/Captions/Image236.html

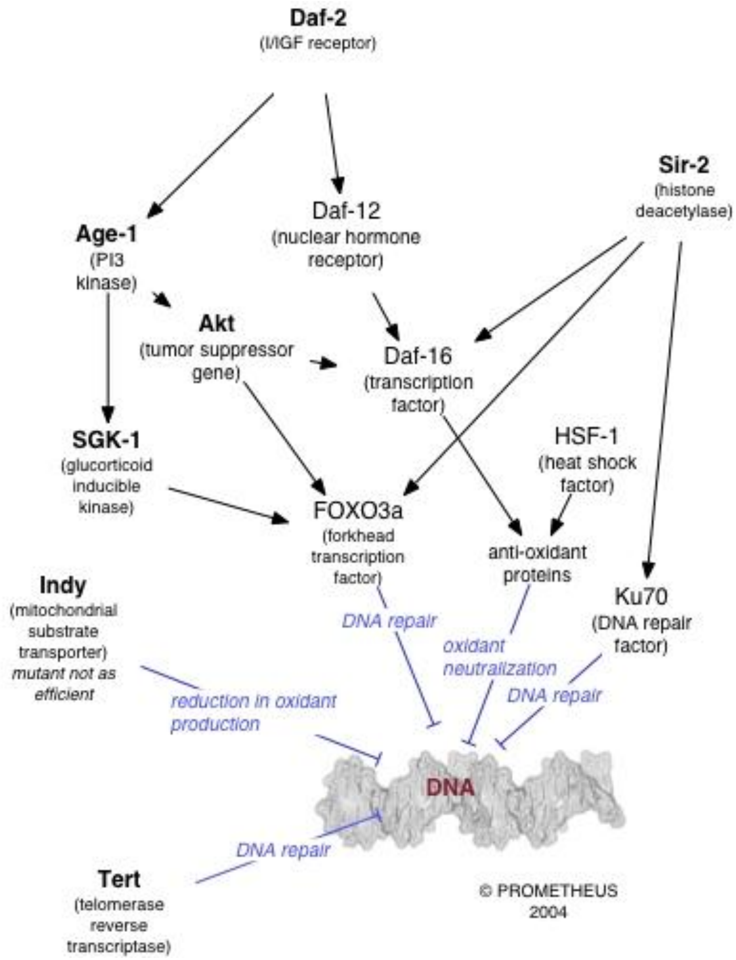

Figure 4. DNA molecules continuously undergo damage from ultraviolet radiation, chemical mutagens, gamma rays and so on. Fortunately, a variety of intracellular DNA molecular repair mechanisms exist that mitigate this problem.

Source: http://en.wikipedia.org/wiki/DNA_repair and http://upload.wikimedia.org/wikipedia/en/a/a6/Dnadamage.jpg

Death, Cryonics, and Future Medical Technologies

A final issue I would like to discuss is an elaboration on the previously discussed hope that future medical technologies might allow for the revival of some individuals previously meeting death criteria. In fact, so confident are some persons that future medical advances will eventually cure almost all diseases that they would be willing to have their body frozen just *before* they would otherwise die of a terminal illness (elective cryo-preservation). They would undertake this with a view to being thawed at some distant future time when there would be a good likelihood of being cured after thawing [19]. For legal reasons, however, the clinically less desirable option of being frozen a brief period *after* asystole has occurred is a far more practical option. In the USA, Alcor, Inc. offers such a service). Candidate patients carry an alert bracelet requesting that as soon as possible after death, a large dose of heparin be given intravenously and the newly dead patient be placed on cardio-pulmonary bypass to allow continuing organ perfusion prior to freezing (Figure 5).


ALCOR
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Figure 5. The bodies or severed heads of 67 "patients" lie in cryogenic storage at the Alcor Life Extension Foundation in Scottsdale, Arizona. Liquid-nitrogen-filled steel containers like this one store up to four "wholebody patients" and six severed heads at −320° Fahrenheit (−196° Celsius). A few years ago, cryobiologists discovered a new preservation process, called vitrification, which virtually eliminates ice-crystal formation. Rather than freezing the tissue, vitrification suspends it in a highly viscous glassy state. In this mode, molecules remain in a disordered state, as in a fluid, rather than forming a crystalline structure. Image Credit: http://news.nationalgeographic.com /news/2005/03/ images/050318_cryonics.jpg. Image legend from: http://news.nationalgeographic.com/news/2005/03/0318_050318 _cryonics.html. Photograph courtesy Alcor Life Extension Foundation.

Two options are offered by Alcor: a whole body option and a less expensive option where only the head is frozen. In either case the hope is that at some future time the body [or head] will be able to be unthawed and repaired, although in the case of the head only option, the problem of finding a matching body exists unless the newly fixed head is repaired to exist as an isolated perfused head in the manner of the incredible isolated head experiments of Professor Bryukhonenko of the former Soviet Union.

(In these grisly isolated dog head experiments the dog had its blood supply to the head isolated, then perfused with blood from a simple heart-lung machine while the head is surgically removed from the body. The resulting isolated perfused dog head (Figure 6) is shown to be conscious to the extent that it responds to various stimuli. A video clip showing parts of the experiment is available online at www.archive.org/details/Experime1940 or at http://www.youtube.com/watch?v=ap1co5ZZHYE. An interesting discussion of the film is available at http://en.wikipedia.org/wiki/Experiments_in_the_Revival_of_Organisms).

Figure 6. This is a screenshot from the controversial film "Experiments in the Revival of Organisms," from the Prelinger Archive. The film is in the public domain. The film depicts Soviet isolated dog head experiments where the dog has its blood supply to the head isolated, then perfused with blood from a heart-lung machine while the head is surgically removed from the body. The resulting isolated perfused dog head remains conscious to the extent that it responds to various stimuli.

Not everyone believes that advocates of cryonics are crazy. For instance, some futurists argue that a number of emerging technologies such as nanotechnology and neuro-prosthetics may eventually allow clinicians to repair brain damage previously believed to be irreversible. Such technologies, if successful, might conceivably even lead to reconstituted personalities in previously brain dead patients, producing a number of clinical, legal and philosophical issues that will require attention. James Hughes puts it this way [18]:

> Ultimately, the nanotechnological neuro-prosthetics that we develop to remediate brain injuries will also lend themselves to the sharing and backing up of memories, thoughts and personalities. That point may be recognized as the "death of death."

Conclusion

In conclusion, this essay has forwarded the notion that the concept of death, previously static for millennia, is now in a process of evolution as biomedical technology advances. In the 1960s the concept of brain death was added to our conceptual armamentarium. We are now working with the notion of non-heart-beating organ donors, where death is declared a mere few minutes after asystole has occurred, but in whom restoration of the heartbeat may still be possible with medical heroics. In the future, developments in cryonics and nanotechnology may force yet another reappraisal, perhaps even to the point where the storing and sharing of memories and personalities may lead to the "death of death."

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