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Break with tradition: donating cadavers for scientific purposes and reducing the use of sentient beings

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Abstract

In recent years, the development of research and the increased awareness of our moral duties beyond the human species have pushed the scientific community to revise widely-accepted ontological reductionist views that regard non-human animals as mere things.
The new horizons offered by the development of advanced research methods therefore require an on-going commitment to new perspectives able to find the right balance between the need for scientific knowledge on one hand and the respect for animal life on the other. This is in line with increasing attention to animal welfare and expansion of the "3Rs model": replacement, reduction, refinement.
With the view of promoting the adoption of alternative methods, human body donation for research can contribute not only to the acquisition of important information for human health and for doctors' training, but also can reduce significantly the number of animals sacrificed.
By investigating the scientific and ethical reasons that may encourage cadaver donation, the authors aim to promote the adoption of the practice in Italy following other European experiences.

Key words

- alternative methods
- cadaver donation
- protection of non-human animals
- animal ethics
- new approaches to animal testing

OLD AND NEW STRATEGIES TO PROTECT NON-HUMAN ANIMALS

With the aim of expanding the application of the "3Rs model" (replacement, reduction, refinement) various establishments have adopted alternative methods (AM) to replace animal experimenting (AE) [1]. Increased interest towards such approaches, several of which have already been validated by the ECVAM (European Centre for the Validation of Alternative Methods) [2, 3] has also prompted their application in highly innovative fields, such as in surgery and microsurgery [4-6]. Both human and animal dummies are used and have attained such a satisfactory level that they almost perfectly simulate the various layers of the skin, including the subcutaneous layers, and internal organs with the possibility of performing operations using cleavage planes applicable to the living[1].

Moreover, diseases that are artificially induced in laboratory animals are never identical to those that occur naturally in human beings and researchers identify numerous difficulties of translating animal data to the patient treatment clinic [7, 8].

The timeframe for developing effective alternative approaches to animal experimentation depends on the availability of economic resources [9].

Development of alternatives to AE are hindered also by the shortage of human tissues and organs.

Conversely, *e.g.* in The Netherlands, there has been such an increase of body donations for medical research and skills training that, in order to avoid a surplus of incoming bodies, several Dutch anatomy institutes have actually decided to decline new registrations [10].

[1]The "bodyform" are models that reproduce the human anatomy and its changes. These are made entirely from synthetic materials that are particularly suitable for use in digestive surgery, urological and gynaecological examination. Each model can be used multiple times. The model "PVC-RAT", which is also entirely made of synthetic material, reproduces the anatomy of rats used so far in microsurgery exercises. This model allows for training in about 25 different microsurgery techniques, such as for example anastomosis, the insertion of a cannula, or the transplantation of blood vessels or organs (www.lscv.ch/it/pages/sperimentazione/alternativi.html).

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In order to increase measures to promote the adoption of alternative, methods, this paper aims to examine the issue of *post mortem* donation of the body as an expression of human solidarity towards not only their peers, but also to living beings in general.

Considerable differences exist throughout Europe concerning body requests for anatomical examination that reflect cultural and religious variations as well as different legal, constitutional and ethical frameworks [11, 12]. As a result, in many European countries, the practice is already applied, whilst in others, such as in Italy, application is problematical.

A recent update on current practice concerning the legal and ethical framework governing Body Donation in Europe has been published by Riederer *et al.* [13]. Particularly, many anatomy departments have developed so called standard operational procedures (SOPs), which are additional rules that go further in the regulation and consideration what constitutes good practice in body donation and the use of human bodies in teaching and research.

In Italy, on the question of donating *post mortem* one's body and tissues, various law proposals[2] were consolidated into one Bill that was debated during the XVI Italian legislature. After successfully passing through the Camera dei Deputati (Chamber of Deputies) on the 19 June 2014[3], it is currently being examined by Italy's upper Chamber, the Senate (paper no. 1534 "Norme in materia di disposizione del proprio corpo e dei tessuti *post mortem* a fini di studio e di ricerca scientifica" (TU unificato C. 100).

The Bill regulates the donation *post mortem* of one's body and tissues for the purpose of scientific research. The donor must expressly declare his/her wishes in a document in the form of a public or private deed. The proposed law also provides that both parents may give consent for the donation of the body of their child. The Ministro della Salute (Italian Ministry of Health), in unison with the Ministro dell'Istruzione, Università e Ricerca (Ministry of Education, Universities and Research) and prior to agreement with the permanent entity responsible for relations between the State, Regions and the autonomous provinces of Trento and Bolzano, shall identify the specialised university and hospital centres to be used for the conservation and use of the bodies for the purposes set out in the law. Furthermore, these centres, which have received the bodies donated for scientific research, shall return them to family members in a dignified manner within two years. The proposed law also establishes that the use *post mortem* of the body and human tissues shall be of a non-profit nature. Costs relating to the transport of the body from the moment of death until the return of the body to family members and burial expenses including any relating to cremation shall be borne by the donee centre.

Our aim, therefore, is in the face of an absence of guidelines and operating procedures to propose a practical guide to reaching an informed decision about body donation.

NEW PERSPECTIVES: MEDICAL TRAINING AND *POST MORTEM* INVESTIGATIONS ON THE HUMAN BODY

The possibility of developing complex initiatives and experimenting new techniques and equipment is an important objective of medical practice in its search to constantly improve healthcare. Basic and specialised professional competences are achieved via precise training programmes that require on a systematic basis advanced knowledge in anatomy[4] [14].

The importance of *post mortem* investigations has been proved by the highly significant data obtained from autopsies carried out on deceased bodies, including those dating back to the distant past, as has emerged in legal cases or anthropological studies performed on mummies or archaeological remains [15-17].

Despite the fact that the system of organ donation is well organized in most European countries, there are no guidelines set out regarding the distribution of non-transplantable material for research purposes [18]. In practice, the distribution of organs and tissue for research purposes is only obtained from inside the hospitals or directly through individual researchers and doctors via personal contacts. It is also important to add that many organs and tissues not suitable for transplants can be very useful for the purposes of research [19, 20].

In strategic research aimed at safeguarding the health of humans, *post mortem* investigation can assume a significant role in a large number of circumstances [21-24]. Sometimes patients may die of metastasis before being able to ascertain the site of the original tumour [25-27]. Awareness of the cause of death of one's own parents and/or of grandparents is important for the offspring, and for the relatives in general, as the origin of diseases, beyond the undeniable effect of the environment, is also influenced by general predisposition and family history [28, 29].

Animal models vs *human organs and tissues in degenerative diseases: the case of multiple sclerosis*

Before patients can be buried or cremated without the cause of death having been discovered, they have to undergo an autopsy [30]. From studies carried out on the brain of deceased patients who had been suffering from multiple sclerosis (MS), it has emerged, for example, that there were traces of a specific virus (the most important seems to be the Epstein-Barr virus, EBV) found in their central nervous systems [31-33]. Multiple sclerosis is an exclusively human disease as animals are never taken ill spontaneously, but rather it occurs

[2]C. 746 Grassi; C. 3491 Magnoli; C. 2690 Brigandi; C. 4273 Di Virgilio; C. 4251 Testa.

[3]During the reading of the Bill in the Chamber of Deputies, the Comitato Nazionale per la Bioetica (National Bioethics Committee) presented an invited submission entitled "Donazione del corpo *post mortem* ai fini di studio e di ricerca".

[4]Practicing new techniques not directly on a living person but initially on cadavers offers a valuable practical opportunity to perform on a human body and tissues without having to resort to using other species. The positive impacts on research, for instance in the area of statistical-based studies, must also be taken into account.

as a result of a series of complex artificial manoeuvres. Recent researches have confirmed that in the study of animal models experimental allergic encephalitis (EAE) therefore produces disappointing and even misleading results [34]. Conversely, the importance of testing on human organs and *post mortem* tissues has been verified by studies conducted at The Imperial College of London, where a bank of human organs and tissues was used by a group of researchers from the Istituto Superiore di Sanità (Italian National Institute of Health) in 2007 [35, 36]. They analysed 22 conserved samples of cerebral material and the results proved a relationship between the presence of EBV and the typical inflammatory reaction of the cerebral lesions present in multiple sclerosis.

Further studies more recently coordinated by researchers at Queen Mary – University of London, confirmed a connection between EBV and MS [37]. According to this research, the EBV virus is involved in the triggering of the neurological disease by means of mechanisms that had not hitherto been demonstrated but only hypothesized. The *post mortem* brain of patients suffering from muscular sclerosis was studied, concentrating on the areas of the brain that had been the most recently subjected to damage. It was discovered that the EBV seemed to have infected the immune cells, prompting an inflammatory process that provoked typical neurological damage. A technique that reveals the presence of brain virus in some MS sufferers, even when the virus is found inside the cells, was utilized for this study. Although EBV is not active, chemical signals are sent through ribonucleic acid (RNA) molecules that activate the immune system causing inflammation and damage to the nervous system and the onset of typical symptoms of MS. The results of this study are potentially very interesting. The way in which EBV is transported to the brain from the immune system has been clarified and the location of the virus at the onset of damage to the nervous system demonstrated. For this research, which also aims to identify the cause, brain tissue was obtained from The Thomas Willis Oxford Brain Collection in Oxford (England), with the informed consent and support of the Ethics Committee.

THE DONATION OF THE HUMAN BODY

The above-mentioned scientific evidence emphasizes and provides proof, as highlighted by many researchers and bioethicists, of the opportunity to promote the *post mortem* donation of human bodies in a similar way to organ donation [38, 39]. In fact, if the explanted organs can contribute to saving or immediately rendering a life more bearable, the donation of corpses and organs for the purposes of research could make a useful contribution to collect varied information to better understand a series of human pathologies.

On the other hand, since organ donation and the cremation of bodies become morally acceptable, the procedure of being "buried whol" has progressively and notably declined. Indeed, currently people are more open to the idea of being "useful to someone" after death [40].

These developments therefore make it necessary to promote a new awareness towards the importance of the donation of one's own body as an expression of human solidarity with regard both to mankind but moreover towards all living beings.

In the light of the limited debate on the issue, along with the absence of guidelines in Italy and a desire for adequate future legislation, the document mentioned below *(see box)* is intended as a guide to offer further information regarding this initiative, in such a way that, while still alive, potential candidates are in a position to choose the most appropriate way of body donation for medical education and research, in accordance with their personal wishes.

Accordingly, we wish to raise awareness of this proposal and obviously institutions, authorities, hospitals and universities can play a key role in disseminating information [39] regarding the opportunity and moral importance of body donation, which is seriously lacking so far. It has to be underlined that donation for research purposes in no way interferes with the donation of organs for transplants as the requirements and timeframes for these donations are different.

The cultural vacuum that currently exists in Italy coexists with the legislative gap the Authors have analysed in the introduction of the paper. In fact, the legal procedure to become a donor fails to regulate adequately issues such as the "ownership" of cadavers, a question on which different views exist, how consent is to be given during the donor's life and which structure has the responsibility for the conservation of the body. The only legal reference points are those regulating the Polizia Mortuaria (Public Mortuary Entity) and an old Decree (Regio Decreto of 31 August 1933) which establishes that bodies not recognised by the deceased person's relatives within six degrees of consanguinity may be used for scientific purposes. Such a regulation, which is still in force, is practically never applied. Moreover, the legitimacy of using unclaimed bodies has exposed vulnerable groups to dissection without their consent [41].

In the absence of a consistent legislative framework, a number of centres for the collection of body donations have been opened and programmes for the donation of bodies and body have been launched [42]. For instance, the Dipartimento di Scienze Biomediche e Neuromotorie – DIBINEM (Department of Biomedical and Neuromotor Sciences) of the University of Bologna covers the expenses of transporting the corpse from the place of death to the Institute in addition to costs relating to the coffin, cremation or burial. Donors or relatives receive no money[5].

The University of Padua promotes body donation

[5]The DIBINEM website offers general guidelines for those wishing to donate their bodies for research and establishes the possible limitations to donation in the case of illnesses or operations undergone. The website also provides a donor consent form in which the donor has to declare whether at the end of the period of study and/or research the body is to be returned to the family for burial or cremation. In the case of cremation, expenses for the return of the donor's ashes to the family will be covered by the Department. By filling in the form, the donor enables the Department to accept the donation of the body. No notarisation of the document is required. However, two adult witnesses must provide their personal details and sign the document. A plaque commemorating the donor if he/she so agrees shall also be produced.

Box 1
Protocol for body donation

I the undersigned

Name and surname:
Place of birth:
Date of birth:
Residence:
Identity document (type: e.g. Identity card):
Identity document number:
Place and date of issue:

In the capacity of donor, I hereby declare the following:
After ascertaining the subject as dead by carrying out an electrotanatogramme and having taken samples of the organs to be transplanted, I leave my body to _____ (*specify the name of the institution to which the body is being donated supplying the relative address*) so that it may be useful to science for whatever clinical and /or scientific experimental activity which from now on will be defined as "Research".
The donation of the body post mortem is exclusively motivated by ethical principles of human solidarity and is inter-specific and entirely free of charge.
The research will be carried out in such a way as to assure the utmost respect for the body.
The results of the "Research" attained will be inserted into a public epidemiological research data bank.
The proof that the certification specifies that body will be used for the aforementioned purposes is a synthesis of the results obtained from the research, and should be handed in to a trustee representative, indicated in the footnotes at the bottom of the page of this document.
Once the procedure is completed in compliance with the terms stated below, the body will be returned to the family members indicated by the undersigned.
Such disposition must not, however, prevent the funeral rights in the form that I have selected.

The "Research" **I agree** _____ **I do not agree** _____ to visibly disfigure my body (mark selected option with an X):
My body **will be** returned to my family in a dignified condition at the end of the "Research", within a maximum period of _____ months for the funeral rights;
My body **will not be** returned and must be _____ (*indicate another option*)

For the implementation of the above the recipient hereby accepts the responsibility of all relative expenses including the transport and the burial of the remains/corpse and/or to require the possible intervention by mortuary officials where such expenses or a part thereof will assume responsibility if covered by local regulations. It will be left to the discretion of the heirs to take responsibility for such expenses or possible additional obligations, subject to notification of the same of the amount foreseen on behalf of the recipient.
In the case of the above-mentioned recipient of neither having the faculties nor the possibility of carrying out the arrangements he will leave the trustee the full responsibility to elect another recipient on the condition that the organization is as similar as possible to those previously established. In the case of difficulty, I authorize the same trustee to annul the hereby document. In the case of inability on behalf of the trustee to act as trustee, I request that such responsibility is assumed by one of my closest relatives, and if this is not possible or is rejected, I request the annulment of this document.
The hereby document does not in any way modify the biological testament ("living will") drawn up by the undersigned.
The above mentioned regulations can be revoked or modified by the undersigned at any moment with a written declaration to this effect, or verbally in the presence of a witness.

I nominate the trustee who must ensure the correct execution of the arrangements Mr./Mrs./Miss:

Born in _____ on _____ Resident in: _____
Address_____ Telephone: _____
Identity document type: (e.g. Identity card): _____
Identity document number: _____
Acceptance of the trustee
_____

Signature: _____

Acceptance of the legal representative from the recipient institute or other structure

Name of the structure/institution:
Date: _____
Name and surname of the legal representative:

Signature: _____

The donor
Place:
Date:

Signature: _____

Note (optional): the hereby document was registered at:
(indicate the details and telephone numbers of others (not the trustee), or professionals such as a solicitor, lawyer, institution or association, etc., where a copy of the hereby document was registered).

through an online explanatory brochure that invites potential donors to contact the University's Clinical Anatomy Centre to fix an appointment during which the objectives and procedures of body donation are explained[6].

Lastly, a very simple donor form exists in Turin, Varese and Arezzo, which however does not address the problems relating to such a choice.

A WORKABLE PROCEDURE FOR BODY DONATION

The proposed donor form template *(see box)* seeks to bring some order to this disparate and incomplete situation.

The use of the human body and/or its parts for the purposes of scientific research raises crucial and much-debated questions on the ethical, scientific and legal significance of death and the role of the principle of an individual's informed self-determination regarding the *post mortem* use of his/her body. Also subject of considerable debate is the issue of brain death, regulated in Italy by Law 578/93 ("Norme per l'accertamento e la certificazione di morte") that came in the wake of the influential Harvard study published in the *Journal of the American Medical Association* in 1969.

Given its moral and scientific complexity together with the many areas of uncertainty that exist [43], the issue should be governed on the basis of the fundamental ethical principles of solidarity and informed self-determination. The recognition of these principles implies that the drafting of legislation regarding the possibility of donating one's body (or parts of it) must address the following points: a) the donor has given expressed consent; b) consent is informed; c) donation has no economic scope.

Recently, also the above-mentioned Italian National Bioethics Committee (NBC) document underlines the need to rigorously respect the principle of donor-informed consent and that in no way does silence give consent[7].

The key points that emerge from the NBC document can be summarised as follows: the donor's freedom of choice and the respect of his/her wishes; the existence of precise rules for body donation; *post mortem* donation for teaching and scientific purposes is a tangible expression of the values of solidarity and the promotion of culture and research aimed at healthcare; the donor's body *post mortem* is to be respected for its connection to the human person and its symbolic and emotional value.

Another essential requirement is that the body donation centres guarantee qualitative standards in the areas of body conservation and the use of bodies for teaching and research that fully respect the dignity of the human person. Furthermore, the centre must specify the scientific aims that the body will be used for.

Although research activity is to be carried out on the body *post mortem* (*e.g.* the use of human tissues), the donor should nevertheless be given all the necessary details to enable him/her to give informed consent.

In other words, in full respect of the principle of self-determination, the donor's consent can only be considered as valid when the information provided to the living donor regarding the intended scientific use of the body and its tissues is specific and detailed. The donor should in fact have the possibility of deciding the aim and method of the scientific activity to be carried out. In this way, the donor can give his/her informed consent and if necessary be sure that sensitive personal information will be protected *post mortem* [44].

We believe that a good law should include this topic. Moreover, according to McHanwell *et al.* [11], a future law should also detail who is the responsible for bequested human remains once the donation has been accepted and specify the length of time for which such remains will be retained by the department or school that accepts them. A good legal framework will ensure that donors have full confidence in the procedures, and so is likely to increase donations. Donors who have bequeathed their bodies for the purposes of anatomical teaching and research should be encouraged to discuss their wills with in order to ensure both that their relatives are clear about their wishes and that their relatives can carry out those wishes expressed in life, after death.

Thirdly, special lectures in ethics relating to the bequest of human remains should be offered to all medical students to encourage the development of appropriate sensitivities in relation to the conduct and respect that is expected in relation to handling human remains used for purposes of professional anatomical education.

Finally, the Ethics Committees can provide important guidelines for authorised centres in the areas of compliance with the donor's wishes and the wider ethical issues relating to the *post mortem* use of the body.

MOVING TOWARDS THE ACCEPTANCE OF *POST MORTEM* DONATION

In revealing the necessity to promote AM, also through the donation of one's own body *post mortem,* it is clearly evident that a culture strongly attached to the centrality of the ego, together with the lack of information/education about these issues, represents a considerable obstacle in accepting that one's own body could become a valuable biomaterial to be "used" by medical science.

Age, education, religion, culture, personality characteristics, view on death and mortality, body image and humanitarian concerns influence people's opinion towards body donation [40] and other factors may all hinder body donation in our country.

The change in attitude of religious authorities to-

[6]The declaration of donation in the donor consent form supplied by the Centre must be completed by the donor, dated and signed. After death, the donor's body is taken to the University of Padua's Centre of Clinical Anatomy to be used for teaching and research by doctors and surgeons. The Centre is responsible for all costs and administrative formalities relating to the organisation and management of the transport of the body. The donor consent form also stresses that the donor receives no payment. Every research project and each single use of the body for teaching purposes is made subject to authorisation given by the person of the Centre in charge, who will ensure that the donor's wishes regarding burial or cremation are respected.

[7]www.governo.it/bioetica/pareri_abstract/Donazione_cadavere_ricerca_20052013.pdf. In the Italian text, it is hoped that the decision to donate is agreed on by family members and that they participate in every stage, including the donor's initial expression of an intention to bequeath his/her body.

wards human dissection has played an important role in relieving public anxiety about these procedures [45].

All major religions, in fact, approve body and organ donation as a charitable act of giving and for medical teaching, research, and transplant. Most major religions support donation as an act of human kindness in keeping with religious teachings.

That statement echoed the Catechism of the Catholic Church, which says in no. 2296: "Organ transplants are in conformity with the moral law if the physical and psychological dangers and risks to the donor are proportionate to the good sought for the recipient. Organ donation after death is a noble and meritorious act and is to be encouraged as a expression of generous solidarity. It is not morally acceptable if the donor or his proxy has not given explicit consent. Moreover, it is not morally admissible to bring about the disabling mutilation or death of a human being, even in order to delay the death of other persons".

Likewise, the catechism states in no. 2301: "Autopsies can be morally permitted for legal inquests or scientific research. The free gift of organs after death is legitimate and can be meritorious". In October 2014, also Pope Francis met with the Transplantation Committee for the Council of Europe and called the act of organ donation "a testimony of love for our neighbour". Nevertheless, researches indicate that people often do not know the attitude that their faith has to the donation or are misled by erroneous interpretation of religious texts or old superstitions [46].

Various researchers [20-22, 47, 48] have shown that young people are more willing to donate their body than older people.

It is also important to understand why individuals who are interested in body donation decide not to complete the registration process [10, 49].

In the investigation of new ways to implement AM we cannot exclude the fact that the level of awareness in existing cultural, social and economic mores is based on the idea of an apodictic legitimacy/inevitability of the exploitation of non-humans. Awareness of an appropriate moral and legal stance towards non-human animals is consequently a long, arduous, and inevitably gradual journey. In recognizing the difficulties, particularly those of a cultural nature, of applying reasons of justice based on inter-specific equality, we remain convinced that in order to make effective headway as far as animal protection is concerned, various differentiated interventions are necessary in order to ensure a realistic grasp of the areas of conflict involved (AE) and the values at play [50].

CONCLUSION

Society accepts that body donation offers a source of health for everybody, but considerable obstacles and resistance continue to limit its widespread use. Potential donors are currently unaware of this possibility. Appropriate information and awareness-raising campaigns are therefore needed through scientific papers, conferences and debates as well as via wider audience channels, such as the mass media in general, that involve not only the medical profession, whose role is nevertheless crucial, but also citizens as a whole. Efforts to enhance donation should seek to identify ways in which potential barriers to donation can be addressed by health professionals. Government should encourage (*e.g.* American and Dutch ceremonies [51, 52]) and promote voluntary donation of one's body and media and other social organisations could make people less hesitant about offering to donate their bodies.

Authors' contribution statement

Alessandro Bonsignore and Susanna Penco equally contributed to this work.

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