REVIEW ARTICLE

Relevant Local *Fatwā* on the Issues of Using Human Tissues in Articular Cartilage Tissue Engineering Experimentation

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ABSTRACT

In articular cartilage tissue engineering (ACTE) experimentation, the researchers have utilised cells and tissues sampled from the human donor for research purposes. The cells and tissues may be harvested from the living donor's discarded tissues through a medical procedure, e.g. the total knee replacement surgery. The small pieces of a tissue sample taken from the human donor are essential to study the articular cartilage regeneration for treating joint disease, i.e. osteoarthritis. However, the procedure has raised some ethical and *fiqh* (Islamic jurisprudence) concerns. The study was done by utilising the secondary analysis of local Muslim jurists' opinions (*fatwā*) related to the sampling of human biological samples. This paper explores the scenarios of using cell sources taken from the living human donor through the existing *fatwā* of local Muslim jurists (*fuqahā'*). The scenarios include: (1) taking samples from the living donor, and (2) discarding human tissue, as practised in ACTE experimentation. The current *fatwā* has shown that honouring every part of a human body is considered essential in Islam. ACTE researchers may utilise the biological samples from living donors as alternatives in studying articular cartilage regeneration. The donation of human biological samples for research purposes in ACTE experimentation, obtained from a medical procedure, may be permissible, should the stipulated terms and conditions were observed, and the procedure does not cause any additional harm to the donor.

KEYWORDS: Articular cartilage, tissue engineering, experimentation, cell sources, Malaysian *fatwā*

INTRODUCTION

The development of scientific knowledge shall be geared to improve the health conditions of society. Perhaps, this is one of the reasons why Muslim jurists had acknowledged the importance of biomedical practices and thus, in principle, agreed on the permissibility of its practices. However, they have also raised some ethical and Islamic jurisprudence (*fiqh*) concerns about the methods used and the implications of biomedical application.[1–5] Despite the great discovery of articular cartilage tissue engineering (ACTE) to treat joint diseases, i.e. osteoarthritis, harm, and therapeutic uncertainties spark the ethical concerns that surround the technology, and this includes the research on the technology itself.[6] Indeed, the ACTE may address the osteoarthritis from five objectives of Islamic law *(maqāṣid al-sharī'ah),* namely, the protection of faith, life, wealth, mind, and offspring.[7] However, Muslim jurists and ethicists may raise concerns about the permissibility *(ibāḥah)* of the ACTE experimentation before the technology is being extensively applied in Malaysia. The issues include the practice of using and disposing of human samples in researches to develop ACTE. Thus, opinions of local Muslim scholars through *fatwā* with regards to the experimentation in ACTE were explored.

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Until now, in Malaysia, there is no specific *fatwā* that has been given on the permissibility of the experimentation of ACTE as the research itself involves a multidisciplinary field with multiple phases and levels from bench to bedside.[8] The issues of using human biological samples in ACTE experimentation can be divided into different scenarios: (1) taking samples from the dead human body, (2) taking samples from the living donor, (3) transplanting human tissue or cells into animal models, and (4) discarding human tissue as practised in ACTE laboratories. In this paper, the present authors focused on the second and fourth scenarios.

The practices in ACTE experimentation can be considered as new emerging issues in *fiqh al-nawāzil*, a branch of Islamic jurisprudence that addresses contemporary issues. Such matters require *fiqh* reasoning (*ijtihād*) based on *uṣūl* (principles and precepts of *sharīʿah*) due to the lack of textual evidence on the upcoming issue. This *ijtihād* is conducted by *fuqahā`* or Muslim jurists who will provide the *sharīʿah* rulings (*aḥkām*) by consulting the primary sources of *sharīah,* which are *al-Qur`ān* and *al-Sunnah*. *Nawāzil* (plural form of *nāzilah*) is characterised by a set of features surrounding the issue, i.e. occurrence, novelty, significance, and severity.[9] However, there are *fatwā* given by local Muslim scholars or *muftī* on specific topics, e.g. organ and blood donation, which can be linked to particular scenarios in ACTE experimentation. There are a total of 15 *fatwā* committees in Malaysia[10] with one at the national level and 14 at the state level (including federal territories). This paper continues to present relevant local *fatwā* of the issues to give a general understanding concerning the permissibility of using and disposing of samples taken from living human donors in ACTE experimentation.

This paper employed mainly the library research method, a process involves identifying and locating relevant information, analysing main points, which lead to developing and expressing the ideas.[11] As stated by George (2008), the library research method "involves identifying and locating sources that provide factual information or personal/expert opinion on a research question".[12] The method may be an essential component of every other research method at a certain time. Subsequently, the study utilised a common research method used by researchers in various disciplines, including communications, history, and health, which is the textual analysis. The data gathered using this method may come from different instruments, e.g. documents and web pages.[13]

In this study, the primary source that was used to screen and retrieve relevant *fatwā* was the Department of Islamic Development Malaysia (*Jabatan Kemajuan Islam Malaysia*) website of *Sumber Maklumat al-Aḥkām al-Fiqhiyyah* or Source of Information on Islamic Jurisprudence Rulings. As of September 2020, there are 604 proceedings of the Consultative Committee of the National Council for Islamic Religious Affairs Malaysia (*Jawatankuasa Muzakarah Majlis Kebangsaan Bagi Hal Ehwal Ugama Islam Malaysia* [JMMKI]) and 2,933 states *fatwā* that are listed on the website.[10] General online searches and websites of *Muftī* Department of each state were also examined to complement the search. Tanzil Project webpage (tanzil.net) – *Yūsuf `Alī* translation and sunnah.com webpage were referred to, for the English translation of Quranic and *Sunnah* sources, respectively. Local *fatwā* related to the sampling of tissue from the human donor was retrieved from the abovementioned sources. The *fatwā* production, which involves the interpretation of primary sources of Islamic law, was described.

Scenario of Taking Sample from the Living Donor for ACTE Experimentation

According to the Cambridge Dictionary (proficiency level)[14], "sample" is defined as "a small amount of a substance that a doctor or scientist collects in order to examine it". Taking samples from the dead human body is related to the term "human biological sample" which is mentioned in the "Malaysian Guidelines on the Use of Human Biological Samples for Research".[15] The term denotes "all biological material of human origin, including organs, tissues, bodily fluids, teeth, hair and nails; but not established cell lines". In ACTE experimentation, there are various types of tissue harvested from the living human patients or donors to test the ability of the cells to regenerate the articular cartilage. These tissues were obtained from human patients after a medical procedure, e.g. total joint

replacement.[16,17] The samples also include various types of stem cells such adipose-derived stem cells[18], bone marrow mesenchymal stem cells[19], placenta-derived mesenchymal stem cells[20], synovium-derived mesenchymal stem cells[21], tooth germs stem cells[22], and umbilical cord blood-derived mesenchymal stem cells.[23] The range of donors' age varied from newborn[24] to 90 years old.[25]

Different from organ or tissue donation for transplantation, the tissues in ACTE experimentation were used for research purposes to investigate and find the cure for joint diseases. However, did the practices violate the *sharīʿah* norm? Or, is the donation of human tissues for research purpose in ACTE experimentation permitted in Islam? Below is the presentation of the relevant *fatwā* related to the cells and tissues sampling from the living donor. The scenario of sampling from the living donor is highly associated with the *fatwā* of organ donation from living donor for therapeutic reasons. For the stem cells used in research, there is a general *fatwā* which can be applied directly for ACTE experimentation.

The transplantation is a medical treatment that is not mentioned explicitly in both *al-Qur`ān* or *al-Sunnah* because the treatment is yet to be introduced during the prophetic time. However, one of the objectives of the organ transplantation is to save lives, which aligned with the *maqāṣid al-sharīʿah*. Indeed, the purpose of the tissue donation in ACTE experimentation is not for therapeutic reasons, but as a research application, whereby the result of the experiments will be used as references for the intended clinical purpose.

In general, Penang *Fatwā* Committee (*Jawatankuasa Fatwa Negeri Pulau Pinang*) (1st August 2010)[26], Johor *Fatwā* Committee (*Jawatankuasa Fatwa Negeri Johor*) (2001)[27], and Sarawak *Fatwā* Board (*Lembaga Fatwa Negeri Sarawak* [JFSarawak]) (1st meeting on 8th-9th December 1995)[28] reiterated that in non-emergency condition, the organ transplantation is prohibited. The transplantation is only permissible in the state of urgency (therapeutic), and giving an honorarium to the donor in the form of payment is not encouraged to prevent organ procurement for trading purpose.

In 1982, JMMKI[29] stated the ruling for blood donation was permissible, and there is no need to isolate or segregate Muslim blood with non-muslim blood. However, similar to the organ donation, any kind of honorarium in the form of payment is not advisable. The *fatwā* is quite general as it did not discuss the requirement of a dire situation as a condition for blood donation:

> *The Muzakarah decided that: 1. The ruling of blood donating is permissible. 2. It is not necessary to separate the blood of Muslims and non-Muslims. 3. An appreciation in the form of money to blood donors is not advisable.*

Meanwhile, the *fatwā* on tissue graft by JMMKI (1995)[30] is straightforward as the committee has issued the use of tissue graft as permissible in medical practices, taken that there is no malpractice of trading. However, the purpose of using tissue graft is only for medical or therapeutic purpose. Meanwhile, JFSarawak (meeting no.1/1995 on 8th – 9th December 1995; meeting no.3/1997 on 18th October 1997)[28,31] agreed on the permissibility of the kidney and other organ donation with stipulated terms and conditions including no trading of the organ.

In contrast, in the issue of uterus donation, all three *fatwā* bodies; JMMKI (106th conference on 21st-22nd October 2014)[32], JFSarawak (27th meeting on 18th November 2015)[33], and Sabah *Fatwā* Council (*Majlis Fatwa Negeri Sabah*) (conference no.1/2016 on 1st-3rd March 2016)[34] agreed on its impermissibility. After being briefed by the researchers from *Universiti Malaya*, JMMKI has concluded that the donation of the uterus is not considered as a necessity (*ḍarūriyyah*) and only act as a complementary (*takmiliyyah*) or embellishment (*taḥsīniyyah*) in family life. The uterus donation is also related to hereditary, which may cause doubtful (*shubhah*) in the lineage. Thus, it can be inferred that the donation of human biological samples for research purposes in ACTE experimentation, obtained from a medical procedure, may be permissible, should the stipulated terms and conditions were observed, and the procedure does not cause any additional harm to the donor, and no trading was involved.

On the other hand, the local *fatwā* bodies derived the consensus and agreed on the permissibility of stem cells

research based on certain conditions. JMMKI (67th conference on 22nd February 2005)[35] and Selangor *Fatwā* Committee (*Jawatankuasa Fatwa Negeri Selangor*) (JFSelangor) (25th May 2006)[36], had examined the stem cells issues and adopted the following resolutions with the same ruling or *ṣīghah*,

> *It is permissible to obtain, develop and utilise the stem cells for medical treatment or lawful scientific research, if the source is also lawful, such as the following: (1). Adults, if they have given permission and they are not exposed to any harm. (2). Children, if their guardians have given permission for some legitimate reason, and at the same time, these children are not exposed to any harm. (3). Placenta and umbilical cord, if the parents have given permission for that. (4). Miscarried foetus, for some lawful treatment purposes, and with the parents' permission, and not with a foetus that was deliberately aborted without any lawful medical reason. (5). Surplus inoculums from the test-tube babies if available and donated by the parents with their permission. Deliberate inoculation of an ovum and spermatozoa of the female and male donors is not permissible based on the principle of sadd al-dharā`i`.*

Apart from that, JMMKI and JFSelangor also had discussed the ruling on therapeutic cloning and stem cell research and come out with the following resolution:

> *(1) Therapeutic cloning for medical treatment, for instance, to create certain cells or to replace damaged organ is permissible. The act is permitted provided that the shari`ah precautions are considered. (2) Using frozen embryo or extra embryo in vitro fertilisation process is permissible for research purpose. However, permission must be granted from the married couple who are under treatment. The research on the embryo must be done before the embryo reach the `alaqah stage (blastocyst). (3) The permission for pre-embryonic research other than therapeutic purposes shall be obtained from the parents. The sample of the research cannot be implanted in the womb of any woman, including the wife. (4) It is permissible to research on pre-embryos to determine the genetic disease of high-risk parents, and the embryo without disease alone may be implanted in the womb of the mother during the period of legitimate marriage. It is impermissible to conduct any research for commercial purpose or unrelated to maternal or fetal health. (5) Genetic engineering treatments on pre-embryos involving the modification of natural human features such as hair, hair colour, intellectual, height, and so on including gender selection is illegal. However, gender selection is permissible, provided the gender factor may cause a serious genetic disease that can lead to death. 6) The research must be conduct legally, and the proposal must be unambiguous and scientifically sound. The research shall be conducted by professional, skilled, trusted and responsible researchers.*

Therefore, it can be concluded that both adult stem cells and embryonic stem cells researches are permissible in Islam as long the *shari`ah* precautions are taken considerably. Assessment on the harvesting technique and procedures to gain the cells may be conducted to reduce the harm inflicted on the donors. Thus, the scientists may conduct the research on stem cells, with terms and conditions, to discover further alternatives for cell sources in ACTE experimentation as the issues have been thoroughly addressed and permitted by the *fatwā* authorities.

Scenario of Discarding Human Tissue in ACTE Experimentation

As cell sources are coming from the human bodies in ACTE experimentation, then, comes the issue of handling the discarded or used cells and tissues after the sampling or analysis. Even though the procedure for handling the human tissue remnants after the experimentation is not mentioned in detail in ACTE studies, the remnants can be treated as clinical samples for disposal.

The issue of discarding and disposal of patients' tissues has been discussed by Kelantan *Fatwā* Committee of Council of the Religion of Islam and Malay Custom (*Jemaah Ulama' Majlis Agama Islam Dan Adat Istiadat*

Melayu Kelantan) (4th July 2004)[37], Islamic Legal Consultative Committee of Pahang (*Jawatankuasa Perundingan Hukum Syarak Negeri Pahang*) (meeting no. 2/2017 on 27th April 2017)[38], JFSabah (conference no. 2/2017 on 23rd-24th May 2017)[39], Negeri Sembilan *Fatwā* Committee (*Jawatankuasa Fatwa Negeri Sembilan*) (conference no. 3/2018 on 29th March 2018)[40], and Islamic Legal Consultative Committee of Federal Territories (*Jawatankuasa Perundingan Hukum Syarak Wilayah Persekutuan* [JFWP]) (*bayān li al-nās* series 170 on 7th March 2019)[41] with various rulings (by citing the four *madhāhib*) and *ṣīghah*. From the given *fatwā*, it can be highlighted that all the committees advise on the burial of the remnants if there is no danger of spreading disease or health hazard. The present author adopted the ruling of disposing of Muslim body parts and tissue as outlined by the JFWP in the following Table 1:

Table 1: Method of discarding human body parts and tissues based on particular situations.

	Situation	Discarding Method
1.	Handling and disposal of Muslim body parts and tissues	**Body parts and tissues of living Muslim** i. According to the majority of jurists, any body parts that are cut off from the living body, including nail or hair, need to be buried without being washed and prayed for. **Body parts and tissues of deceased Muslim** i. According to *al-Ḥanafi* and *al-Mālikī* schools, if a large part of the corpse were to be found, it must be bathed, shrouded, prayed for, and buried. ii. For *al-Shāfi'ī* and *al-Ḥanbalī* sects, the deceased must be bathed, shrouded, prayed for, and buried even only a small part of the corpse is found.
2.	Handling and disposal of non-muslim body	It should be buried or cremated according to the religious teachings of the deceased.
3.	Handling of body parts and tissues which are a health hazard and may contaminate the environment	i. The organs and tissues removed and cut off from the patient's body, either Muslim or non-muslim patients should be buried. ii. If the organs or tissues are contaminated with infectious diseases, then the hospital should decontaminate them with certain chemicals before burying them. iii. If there are no other alternatives to decontaminate the organs and tissues, it is permissible to incinerate them based on the principle of *ḍarūriyyah* .
4.	Handling of Muslim fetus	**a. The fetus survived for a moment when it was born** i. If it lived for a short while after being born, it should be given a name, bathed, and prayed for. It also has the right to inherit and to be inherited of its property based on the relevant *fiqh* just the same as the other living person. ii. In *al-Shāfi'ī* sect, if the baby was crying during birth delivery and it was certain, it was being alive by signs of life (there was a movement etc.), then it is required for the baby to be bathed, shrouded, prayed for, and buried just like adult's funeral. **b. The fetus died at birth (stillbirth)** i. According to *al-Ḥanafi* sect, if the fetus is stillborn, and there is no sign of life, it must be bathed, named, shrouded in a piece of cloth, and buried without prayer. ii. For *al-Mālikī* sect, a stillborn baby without any signs of life such as crying (baby's movements are not considered as a sign of life), it is not necessary to bathe the deceased. According to *Ibn Shihāb*, the stillborn baby need not be prayed for, but it can be buried with its deceased mother. iii. If the baby was not crying during the labour and the age is not up to four months, then it is not an obligation for it to be bathed, shrouded, and prayed for. However, it is recommended (*mandūb* or *mustaḥabb*) for the baby to be shrouded and buried without being prayed for. iv. In *al-Ḥanbali* school, as mentioned by *Ibn Qudāmah*, if the fetus had reached the age of four months or had a perfect body form, thus it should be bathed and prayed for although there are no signs of life and it is recommended to give a name to it.
5.	Existing regulation of handling and disposal	i. Based on the current practice, the concessionaire will dispose of the chemical and clinical waste, including human tissues, organs, and fetuses through incineration. ii. Under the proposal to bury chemical waste containing formalin and other chemicals, the Ministry of Health Malaysia has discussed the matter with the Department of Environment. The department suggested that the materials should be buried in an area with 100 meters away from the water source. Also, it is recommended that the burial site to be adjacent to the existing graves as long as it is away from water sources, residential areas, wells and dams.

At the moment, as highlighted by JFWP[41], the current practice of Malaysian hospitals is that the disposal of the "clinical waste" is done by incineration which handled by concession companies (Radicare Sdn. Bhd., Faber Medi-Serve Sdn. Bhd., and Pantai Medivest Sdn. Bhd.) which is responsible for the disposal of the hospitalisation process at the hospital premises to the incineration process. While the disposal of "chemical waste" is done by the Concession Company Quality Nature Sdn. Bhd. JFWP[41] concluded that the current practice of "clinical waste" disposal is not considered in line with the *sharīah* unless there is an urgency to do so. The practice may also be applied in the case of ACTE experimentation whereby the concession company will collect the clinical waste to be discarded. Thus, the researchers need to improve the standard operating procedure in discarding the clinical waste in ACTE research to be in line with *sharīʿah*.

CONCLUSION

In searching for the treatment for degenerative joint diseases, the researchers of ACTE have been utilising human tissues as the cell sources. The tissues were sampled from the living donor from different parts of the body, and various types of cells were harvested. Due to this method of using human samples are widely accepted in ACTE experimentation, there is a need to screen the practices from an Islamic perspective, through the analysis of relevant *fatwā*. Verily, the experiments are essential to developing a new treatment in the tissue engineering field to produce functional articular cartilage tissue. However, it is far more important for the researchers to ensure their conduct to be in line with the *sharīʿah*. ACTE researchers are advised to refer to the *fatwā* committees or religious bodies before adopting or adapting the international biomedical practices, before implementing the technology in Muslim societies, i.e. Malaysia. The *fatwā* can be used as references for the researchers in conducting their studies, to be in line with *sharīʿah*. In conclusion, ACTE researchers may utilise the biological samples from living donors as alternatives in studying articular cartilage regeneration. The donation of human biological samples for research purposes in ACTE experimentation, obtained from a medical procedure, may be permissible, should the stipulated terms and conditions were observed, and the procedure does not cause any additional harm to the donor. Besides, the current standard operating procedure of discarding the clinical waste in ACTE research needs to be improved, so that, the procedure to be in line with *sharīʿah*. Despite new efforts to align researches in ACTE with the *sharīʿah*, further study needs to be done to develop a permissible (***ḥalāl***) environment of ACTE experimentation.

CONFLICT OF INTEREST

The authors in this study declare that there is no conflict of interest.

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