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## **Regeneration of Human Body Parts via Tissue Engineering and Regenerative Medicine: A Brief Insight into the Technology from Islamic Perspective**

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### **Abstract**

Tissue engineering and regenerative medicine (or, T.E.R.M.) field has been progressing well during the last few decades. Most of T.E.R.M. related studies indicated promising research findings in tissue reconstruction and regeneration. Successful tissue reconstruction and regeneration requires a great balancing acts of the three T.E.R.M. elements or principles namely (1) quality cells source, (2) appropriate biomaterial scaffolds and (3) adequate signalling factors i.e. physical and/or chemical stimuli. From its theoretical framework, this multidisciplinary biomedical technology will enable us to restore, delay or even reverse the aetiology of diseases. It is anticipated that T.E.R.M. will augment current practices in tissue or organ transplantations. It would serve as a potential solution for the lack of tissues or organs donor. Taking advantage of a fully autologous system or approach, T.E.R.M. will help minimize the risk of infection and the issues of rejection (or, adverse host reaction). It is expected that millions of people would be benefited from T.E.R.M. in the near future. This initiative is worth to explore and must be given due consideration by Muslims since there are growing demands for a *shari'ah* compliance biomedical application. Despite much hopes and expectations, T.E.R.M. has been confronted with some questions arising from the social, cultural and/or religious implications of this new-found knowledge and technology. Based on the available literatures, most of the countries around the world support this highly technical T.E.R.M. research for it is rapidly advancing the understanding of the human tissue regeneration. Although T.E.R.M. is potentially beneficial to improve the health of people, this newly found technology can also be misused. In some cases, it is difficult to differentiate whether T.E.R.M. falls under a pure scientific research or a medical technology innovation that can be applied directly onto patient. The choice in relation to scientific or legal aspects could raise ethical dilemmas as well as religious issues. It affects various stakeholders i.e. patients, medical professionals, and public at large. In order to address the complexity, this present paper intends to explore the principles of T.E.R.M. in terms of tissue regeneration aspects in modern science and Islam, based on the two sources of knowledge i.e. the *Qur'an* and *Hadith* (sayings and actions of the Prophet S.A.W.). Emphasis is given on the usage of foreign materials as well as the issues of seeking best treatment and utilizing unlawful things. Refraining from giving an ultimate Islamic decree, the approach is taken to nudge or instigate a discussion on certain issues pertaining to research and application of T.E.R.M. which is still under-represented. Initiation on the foundation of the subject should be ventured further. It is also hoped that the content of this paper will be well received by the readers, and the brief discussion will be enlightening and educational for those who are interested in this important subject.

**Keywords:** *Tissue engineering; regenerative medicine; cells; biomaterials; signalling factors; regeneration, Islamic perspective.*

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## **Abstrak**

Bidang kejuruteraan tisu dan perubatan regeneratif (atau, T.E.R.M) telah berkembang dengan baik dalam tempoh beberapa dekad yang lalu. Kebanyakan kajian T.E.R.M. yang berkaitan telah menunjukkan hasil penyelidikan yang menggalakkan dalam pembinaan semula tisu dan pertumbuhan semula. Pembinaan dan pertumbuhan semula tisu yang berjaya memerlukan tindakan keseimbangan yang besar terhadap tiga elemen T.E.R.M atau prinsip-prinsip yang dikenali sebagai (1) sumber sel-sel yang berkualiti, (2) perancah bahanbio yang sesuai dan (3) faktor isyarat yang mencukupi iaitu rangsangan kimia dan/atau fizikal. Melalui rangka kerja teori, pelbagai disiplin teknologi bioperubatan membolehkan pemulihan, kelewatan atau menyongsangkan etiologi penyakit. Jangkaan perubahan T.E.R.M. akan meningkatkan amalan semasa dalam transpindahan tisu atau organ. Ia akan menjadi satu penyelesaian yang berpotensi kerana kekurangan tisu atau organ penderma. Dengan mengambil kesempatan daripada sistem autologous sepenuhnya atau pendekatan, T.E.R.M akan membantu mengurangkan risiko jangkitan dan isu-isu penyingkiran (atau, reaksi perumah). Ia dijangka bahawa berjuta-juta orang akan mendapat manfaat daripada T.E.R.M dalam masa terdekat. Inisiatif ini adalah bernilai untuk dikaji dan perlu diberi perhatian oleh umat Islam kerana terdapat peningkatan permintaan untuk pematuhan syari'at dalam aplikasi bioperubatan. Walaupun terdapat harapan, T.E.R.M. telah berhadapan dengan beberapa soalan yang timbul daripada implikasi sosial, budaya dan / atau agama terhadap pengetahuan teknologi baru yang ditemui. Berdasarkan kesusasteraan yang ada, kebanyakan negara-negara di seluruh dunia menyokong penyelidikan teknikal T.E.R.M kerana ia cepat meningkatkan pemahaman pertumbuhan semula tisu manusia. Walaupun T.E.R.M. berpotensi memberi manfaat untuk meningkatkan kesihatan manusia, teknologi baru ditemui ini juga boleh disalahguna. Dalam beberapa kes, ia adalah sukar untuk membezakan sama ada T.E.R.M terbahagi di bawah kajian saintifik tulen atau inovasi teknologi perubatan yang boleh digunakan terus pada pesakit. Pilihan yang berkaitan dengan aspek saintifik atau undang-undang boleh menaikkan dilema etika serta isu-isu agama. Ia memberi kesan kepada pelbagai pihak yang berkepentingan iaitu pesakit, profesional perubatan, dan masyarakat umum. Dalam usaha untuk menangani kerumitan, kajian ini bercadang untuk meneroka prinsip T.E.R.M dari segi aspek pertumbuhan semula tisu dalam sains moden dan Islam, berdasarkan dua sumber ilmu iaitu al-Quran dan Hadis (perkataan dan tindakan Rasulullah SAW). Penekanan diberikan kepada penggunaan bahan-bahan asing dan isu-isu yang mendapatkan rawatan terbaik dan mengguna pakai perkara yang menyalahi undang-undang. Menahan diri daripada memberikan satu perintah Islam muktamad, pendekatan itu diambil untuk menggerakkan atau menghasut perbincangan mengenai isu-isu tertentu yang berkaitan dengan penyelidikan dan aplikasi T.E.R.M yang masih kurang dikaji. Permulaan asas subjek perlu diteroka dengan lebih lanjut. Ia juga berharap bahawa kandungan kajian ini akan diterima baik oleh pembaca, dan perbincangan ringkas akan menyedarkan dan mendidik untuk mereka yang berminat dalam mata pelajaran penting ini.

**Kata kunci:** *Kejuruteraan tisu; perubatan regeneratif; sel; bahan bio; faktor isyarat; pertumbuhan semula, perspektif Islam.*

## **Introduction**

Tissue loss or end-stage organ failure resulting from injuries, diseases or ageing is seen as a major dilemma in healthcare. Available treatment options such as tissue/organ transplantation (e.g. human or xenotransplantation), surgical repair, artificial prostheses, mechanical devices, as well as drug therapy do not repair and restore the tissue/organ function. In fact, most of them are not intended to integrate with the host tissue. Moreover, mechanical devices or artificial prostheses may be subjected to wear upon long-term implantation, and could induce inflammatory response in the host (Chapekar, 2000). These multitude shortcomings have paved the way for T.E.R.M. to facilitate the regeneration of damaged tissues or organs (Rahman et al., 2015; Tabata, 2009). Indeed, this initiative is worth to explore and must be

given due consideration by Muslims since there are growing demands for a *shari'ah* compliance biomedical application.

Despite much hopes and expectations, T.E.R.M. has been confronted with questions arising from the social, cultural and/or religious implications of its new-found knowledge and technology. This innovative medical biotechnology, although potentially beneficial to improve the health of people, can also be misused. Besides, in certain aspects of application, it is rather difficult to distinguish whether T.E.R.M. is a pure scientific research or a medical technology innovation. At the moment, medical items fall under the medical technology innovation by-pass the whole range of validation procedure and can be applied directly onto patient (Eaton & Kennedy, 2007). The choice in relation to scientific application

and/or legal aspects could raise religious and ethical dilemmas that affect various stakeholders i.e. patients, medical professionals, and public at large.

In order to address the complexity, this paper intends to explore some principles of T.E.R.M. in terms of tissue regeneration aspects in modern science and *Islam* - based on the two sources of knowledge i.e. the *Qur'an* and *Hadith* (sayings and actions of the Prophet S.A.W.). Emphasis will be given on the usage of foreign materials as well as the issues of seeking best treatment and utilizing unlawful things. In the spirit of pursuing and producing beneficial knowledge for Muslims, this paper attempts to provide the foundation of the subject based on the authors' experience in T.E.R.M. Refraining from giving an ultimate Islamic decree, the approach of this paper is initiate discussion on certain issues pertaining to research and application of T.E.R.M which is still yet to be explored. There is a need to fill the gap. It is hoped that the content of this present paper will be enlightening and educational for those who are interested in performing the *ijtihad* on this important subject.

## **Tissue Engineering and Regenerative Medicine: The Technology**

### **I. Brief History and Origins**

There is no consensus on the exact origin of the term 'tissue engineering'. The first recorded use of the term was in an article on 'Functional Organ Replacement: The New Technology of Tissue Engineering' in 1991 (Vacanti, 2006). However, the term may arise in the late 1980s (Vacanti, 2010). In a more recent article, the authors claimed that Dr. Fung, from California University suggested the term during the National Science Foundation Meeting in 1987. While in 1988, O'brien (2011) reported that National Science Workshop officially coined the 'Tissue Engineering' term as, "*the application of principles and methods of engineering and life sciences toward the fundamental understanding of structure-function relationships in normal and pathological mammalian tissues and the development of biological substitutes to restore, maintain or improve tissue function.*"

Although the specific terminology arouse only about 30 years ago, the idea of replacing tissues goes back to 16<sup>th</sup> century. Gasparo Tagliacozzi (1546-99), a Professor of Surgery and Anatomy at the University of Bologna described a nose replacement constructed from a forearm flap in his work; 'The Surgery of Defects by Implantation' (*De Custorum Chirurgia per Insitionem*) which was published in 1597. On the other hand, human limb transplantation can be traced back to almost 300 A.D. with the famous painting of

'Healing of Justinian'. This painting visualized the legend of St. Cosmas and St. Damien depicting the transplantation of a homograft limb onto an injured soldier (Meyer, 2009).

In some literatures, tissue engineering is viewed as a tool or a subset for regenerative medicine. However, unlike tissue engineering, 'regenerative medicine' term is less defined in the literatures. Lysaght & Crager (2009) found the term used by Leland Kaiser for the first time in a 1992 article on hospital administration and discredit the attribution to William Hazeltine as thought to be the founder of the term.

Most biologists and physicists relate regenerative medicine specifically on stem cell induction of reforming damaged tissues and organs in human. The technology seeks to develop functional cell, tissue, and organ substitutes to repair, replace or enhance biological function that has been lost due to congenital abnormalities, injury, disease, or ageing. It includes both the regeneration of tissues *in vitro* for subsequent implantation *in vivo* as well as regeneration directly *in vivo* (Brown, 2013). Ultimately, the aim of regeneration is to restore both structure and function of tissues/organs (Mason & Dunnill, 2008).

The use of the 'tissue engineering' term is quite synonymous with the term 'regenerative medicine' though the latter does not involve seeding cells onto scaffold. They have been used interchangeably by researchers in the field thus far. As a matter of fact, both terms are even combined and known as Tissue Engineering and Regenerative Medicine (T.E.R.M.). The field has grown substantially over the past few years. Nearly 4000 original articles published in 2010 compare to lowly 360 ten years earlier. Simple search for the keywords 'tissue engineering' or 'regenerative medicine' hits to more than 28,000 original articles and 6000 review articles in Scopus database (Fisher & Mauck, 2013). From the literatures, most countries in the world supports this highly technical T.E.R.M. research for it is rapidly advancing the understanding of the human tissue regeneration. If this know-how technology is successful, it is anticipated that millions of people including Muslims population would be benefited from the application.

### **II. General Principles**

General principles of T.E.R.M. involve cells source, biomaterial scaffolds and signalling factors (Figure 1). The three components are also known as tissue engineering triad (Murphy et al., 2013; Sha'ban et al., 2014). A successful Tissue Engineered Medical Products (or, T.E.M.Ps) require quality cells sources to facilitate tissue formation. While compatible

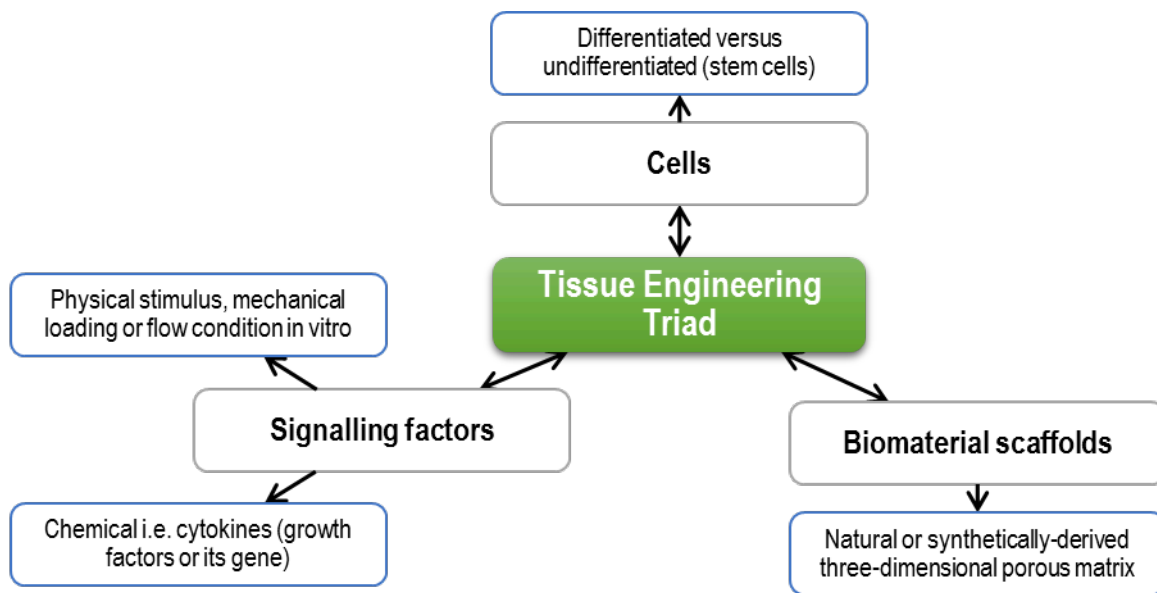


Figure 1: 'Tissue engineering triad' represents the principles of tissue engineering (Sha'ban et al., 2014).

biomaterial scaffolds provide a conducive 3D microenvironment for cells and tissues growth, appropriate signalling factors promote or enhance the cells proliferation as well as their differentiation *in vitro*.

The source of cells used in T.E.R.M. can be autologous (i.e. from the patients themselves), allogeneic (i.e. from a human donor but, not immunologically identical), or xenogeneic (i.e. from a different species) (Koh and Atala, 2004). The types of cells can be categorized based on differentiated and undifferentiated cells. The differentiated cells are usually referred to as mature primary cells; or adult progenitor cells; or committed cells. They are specific to tissue types that are harvested from patients own tissue. The advantage of differentiated cells is due to its potential to overcome immune rejection. Being differentiated, the cells require no substantial manipulation in *in vitro*. However, the yield and proliferation of cells derived from certain tissues tend to be quite low in average. Hence, this may not be a good option for some tissues (Polak & Bishop, 2006). In contrast, the undifferentiated or uncommitted cells (also known as stem cells) have the ability to differentiate to one or many types of specialized cells. The differentiation is induced using a relevant signalling factors specific to the growth of intended cells. Numerous researches deviate and give more attention to stem cells due to its availability and differentiation plasticity (Howard et al., 2008; Satija et al., 2009; Steigman et al., 2008). However, the induction steps for cells differentiation involve

substantial *in vitro* manipulation of the stem cells with no or little known long-term effects (Sha'ban et al., 2014).

Biomaterial scaffolds can be natural (e.g. collagen, fibrin and alginate), acellular tissues (e.g. bladder submucosa and small intestinal submucosa) and synthetic polymers (e.g. polyglycolic acid [PGA], polylactic acid [PLA], and poly(lactic-co-glycolic acid) [PLGA]). Choosing appropriate scaffolding material is important since each group of scaffolds has its own advantages and disadvantages (Mohamad et al., 2014a, b). Natural and acellular scaffolds had been reported to have better biological recognition. While synthetic polymers have the ability to control the properties of microstructure, strength and degradation rate (Atala, 2012). The success of the scaffolds depends on several factors that include bulk materials, three-dimensional architecture, porosity, surface chemistry, mechanical properties, initial scaffold environment (e.g. osmolarity and pH), as well as degradation characteristics (Chan & Leong, 2008).

Signalling factors can be physical and/or chemical stimuli. As important as biomaterial scaffolds, the signalling factors facilitate and direct cells growth in *in vitro*. Physical stimuli usually involve mechanical loading or flow condition in a bioreactor (e.g. CO<sub>2</sub> incubator, spinner flask etc.), which can direct or indirectly in contact with the cultured cells. On the other hand, for chemical stimuli, the reagents or substances (e.g. growth factors and/or its genes) are supplied to the cells through culture media that has a

direct contact with the cells. While for the genes, they are usually transferred into the cells to enhance the properties by means of molecular cloning. This set of experiment step implies substantial cells manipulation in vitro. The outcomes are positive so far, but then again, there is no or little unknown (if any) long term effects (Mohamad et al., 2014c; Sha'ban et al., 2014).

## Islamic Perspective

### I. Islamic Sources and Jurisprudence

Global estimate account 1.57 billion Muslim in 2009 with nearly one in four of the world's 6.8 billion inhabitants (Grim & Hsu, 2011). The consensus faith of every *Muslim* is to believe in one God; *Allah* and Prophet *Muhammad* (peace be upon him; pbuh) as final messenger of God. The *Qur'an*, the word of God transmitted to Prophet *Muhammad* (pbuh) in the span of 23 years via direct communication or through intermediacy of Archangel Gabriel (*Jibreel*). The *Qur'an* is the ultimate source in *Islam*, encapsulating its message and being the foremost guidance as well as legislation in *Muslim* lives (al-Amri, 2010). The uniqueness the *Qur'an* lies in its tremendous verbatim memorization and preservation even after 1400 years. Sir William Muir, one of the foremost critics of *Islam* in 18<sup>th</sup> century admitted perhaps none other book than the *Qur'an* has the utmost text preservation (Muir, 1894).

The second important source in *Islam* is the *Hadith* (or, the *Sunnah*), an oral and practical commentary of the *Qur'an*. The *Hadith* is defined as transmission on the authority of the Prophet *Muhammad* (pbuh), his deeds, sayings, tacit approval or description of physical appearance (A'zamī & A'zami, 1977). In terms of legal methodology (*usul al-hadith*), the *hadith* refers to only the statements, acts and approvals of the Prophet (Philips, 2007). Based on these sources, *Muslim* scholars have developed methodology for interpreting the law that lead to the rise of different school of thoughts which also known as *Madhhab*. Common school of thoughts in *Sunni* world are *Maliki*, *Hanafi*, *Syafie* and *Hanbali*. These school of thoughts formulated Islamic jurisdiction referring to the *Qur'an* and *Hadith* as well as using opinion of companions of the Prophet *Muhammad* (pbuh), *al-Qiyas* (logical reasoning), *al-Istihsan* (legal preference) and *al-uruf* (custom). Note that variation in the acceptance and rejection of the secondary sources cause differences in the formulation of Islamic jurisprudence. Thus, no single *Madhhab* can perfectly be claimed to represent *Islam* as a whole instead all have been important instruments for the clarification and application of the Islamic jurisprudence (Philips 2006).

Islamic jurisprudence or *Fiqh* is closely associated with the *Muslim* ways of life. It covers practically all aspects of a man's life. Islamic legal rulings include obligatory (*Wajib*), desirability or recommended (*Sunnah*), simple permissibility (*Harus*), undesirability or offensive (*Makruh*) and prohibition (*Haraam*). These five (5) Islamic legal rulings serve to guide man in dealing with their daily activities and issues. The application of these rulings is to achieve benefits, preventing harm and maintaining order and justice to mankind (Mohamad et al., 2014c).

### II. Regeneration Concept

Needless to say, modern science has achieved remarkable success in the field of T.E.R.M. though many challenges are still waiting to be overcome in the near future. At the moment, several tissues and organs (e.g. full facial, double arms, windpipe or the trachea, urethra, bladder, skin etc.) have been successfully implanted and regenerated in human (Orlando et al., 2011). However, T.E.R.M. has yet to overcome the hurdle of complete body regeneration e.g. in the case of "missing" organs. Unlike salamanders that can regenerate its full body part (i.e. the limb), human are not able to regenerate perfect replacements for lost body parts (Muneoka et al., 2008).

The concept of regeneration in *Islam* is more comprehensive than what has been achieved in modern science. Islamic doctrine views that human existence continues after the death of the human body in the form of spiritual and physical body regeneration. The afterlife involves rewards and punishments which are commensurate with earthly conduct. Every deeds performed in this life will be judge accordingly in the hereafter. The *Qur'an* states in respond to the non-believers, *The Unbelievers think that they will not be raised up (for Judgment). Say: "Yea, By my Lord, Ye shall surely be raised up: then shall ye be told (the truth) of all that ye did. And that is easy for Allah."* (The *Qur'an* 64:7). *Allah* explicitly addresses the rejection by non-believers on the idea of resurrection. *Allah* also says, *"O mankind! if ye have a doubt about the Resurrection, (consider) that We created you out of dust, then out of sperm, then out of a leech-like clot, then out of a morsel of flesh, partly formed and partly unformed, in order that We may manifest (our power) to you; and We cause whom We will to rest in the wombs for an appointed term, then do We bring you out as babes, then (foster you) that ye may reach your age of full strength; and some of you are called to die, and some are sent back to the feeblest old age, so that they know nothing after having known (much), and (further), thou seest the*

earth barren and lifeless, but when We pour down rain on it, it is stirred (to life), it swells, and it puts forth every kind of beautiful growth (in pairs) (The *Qur'an* 22:5).

Allah promises eternal life for human being in afterlife, either promoted to paradise or condemn permanently to hellfire. The condemnation of non-believers leads to the view of specific regeneration of human body involving skin. The inhabitants of hellfire will be continuously cast into hellfire and their skin will be constantly regenerated. *Those who reject our Signs, We shall soon cast into the Fire: as often as their skins are roasted through, We shall change them for fresh skins, that they may taste the penalty: for Allah is Exalted in Power, Wise.* (The *Qur'an* 4:56).

The *Qur'an* further states the miracle capability of Prophet *Isa* (pbuh) in resurrecting the dead in this world (The *Qur'an* 3:49). This view is similar to Christianity. The Bible mentioned the event explicitly in Gospel of John regarding Lazarus (John 11: 1-46). *Islam* associates the ability of resurrecting dead body to Allah alone. While, Christianity attributed it to Prophet *Isa* (pbuh) himself since he is considered as son of God or God himself.

The *Hadith* mentions numerous narrations with regards to specific body regeneration. In the ultimate journey of *al-Isra' wa al-Mi'raj*, Prophet *Muhammad* (pbuh) ascended to the seven heavens to meet Allah, the Exalted is He. Extraordinary vision was given to Prophet *Muhammad* (pbuh) where he passed by a group who neglected prayer. Their heads were crushed by boulders and again resume their shape only to be crushed again. This process would continue unabated (*Sahih al-Bukhari, Hadith No. 1386*). The first woman created from Adam's ribs mention in the *Hadith* exhibits unique form of regeneration. No scientific explanation able to comprehend regeneration of woman from man. In spite the view of regeneration, this narration has become a polemic and spark debate among Muslim scholars. Majority of classical *Muslim* exegesis supported the narration literally while others interpreted it metaphorically (Ramli et al., 2013).

### III. Foreign Materials: Seeking Best Treatment

Important issues involving abortion, genetic engineering, organ transplant and euthanasia received a lot of attention from the *Muslim* communities (Mohamad et al., 2014). Less emphasis is given on the study of material used in Islamic history. Up to date, no known publication discussed thoroughly and specifically the type of material and the technology practice in Islamic history. The knowledge on the

type of material used in the past is vital since it may impact the regulation of Islamic jurisprudence in the field of T.E.R.M.

Utilization of synthetic material replacing missing parts of human body is not something new in Islamic world although application of tissue engineering (cell seeded onto scaffold) was absent. Study on Islamic literature demonstrated the usage of synthetic material replacing missing parts since the time of Prophet *Muhammad* (pbuh). Abu Daud al-Sijistani (died 889CE) recorded in his book, *Sunan Abi Daud* from 'Urfajah ibn As'ad the permissibility of using gold to replace the missing nose. He narrated in his book on the authority of AbdurRahman ibn Tarafah that he said that his grandfather 'Urfajah ibn As'ad who had his nose cut off at the battle of *al-Kilab* got a silver nose, but it developed a stench, so the Prophet *Muhammad* (pbuh) ordered him to get a gold nose (*Sunan Abi Daud, Hadith No. 4220*).

Contextualizing this narration in our modern perspective allow extrapolating the permissibility to seek best treatment available at our time for a specific disease. At that particular time, synthetic materials as bioimplants made from gold was the best treatment to treat the missing nose. At our time, engineered tissue cultured on biodegradable scaffold consider as better alternative for the deficient in the medical implant. The use of gold as the material for bioimplant in this case initiates the debate on the utilization of illegal (*haraam*) material in medicine. *Islam* forbids the use of unlawful (*haraam*) material except in case of no alternative or in dire necessity. Abu al-Darda narrates Prophet *Muhammad* (pbuh) said, "Indeed Allah has sent down both illness and it's cure, and He has appointed a cure for every illness, so treat yourselves medically, but use nothing unlawful" (*Sunan Abi Daud, Hadith No. 3874*). Tariq ibn Suwayd asked the Prophet *Muhammad* (pbuh) regarding wine for medicine and it was not allowed (*Sunan Abi Dawud, Hadith No. 3873*).

The contradictory narrations must be contextualized properly. *Haraam* things are not forbidden when no alternative are present (Ibn Adam, 2004). Specific instances have been recorded when the companions of Prophet *Muhammad* (pbuh) reported to use the urine of camel and silk for medical treatment. Anas bin Malik, a companion of Prophet *Muhammad* (pbuh) narrated that some people from the tribe of 'Ukl felt ill and commanded by the prophet to drink the urine and milk of the camel for medicine purposes (*Sahih al-Bukhari, Hadith No. 6805*). The Prophet permitted Zubair and Abd al-Rahman to wear silk to treat itching of the skin although wearing silk is forbidden for male (*Sahih al-Bukhari, Hadith No. 5839*).

## Conclusion

Tissue Engineering and Regenerative Medicine (T.E.R.M.) is a promising biomedical research field in tackling the issue of artificial implant and tissues/organs donor deficiency. A great balancing acts of the three T.E.R.M. principles namely quality cells source, biomaterial scaffolds and signalling factors i.e. physical and/or chemical stimuli will ensure the success tissue reconstruction and regeneration. Taking advantage of the autologous system, T.E.R.M. will minimize the risk of infection and the issues of rejection in patients.

The future application of T.E.R.M. will involve *Muslims* community thus, the connection between Islam and the T.E.R.M. is worth to be examined. Several uncertainties and unanswered questions from both empirical (e.g. the actual requirements and mechanisms for tissue regeneration) and social (e.g. religious and ethical challenges) aspects remain ambiguous to the field. Modern science enables great success in replacing tissues and organs up to certain level but has yet to achieve complete regeneration of the human body. While Islamic sources exhort believe in human regeneration including specific body parts.

Islamic history demonstrated the permissibility of using synthetic material for bioimplants and seeking the best treatment for a particular disease. Unlawful materials only be used in dire situation with the absent of alternative treatment. A Qur'anic verse that implies this can be found in the *Qur'an* where Allah says, "He hath only forbidden you dead meat, and blood, and the flesh of swine, and that on which any other name hath been invoked besides that of Allah. But if one is forced by necessity, without wilful disobedience, nor transgressing due limits - then is he guiltless. For Allah is Oft-forgiving Most Merciful." (*The Qur'an* 2:173).

The concept of Evidence Based Practice specified that no intervention shall be applied to the patients unless the benefits are proven to outweigh the risks. It was narrated from 'Amr bin Shu'aib, from his father that his grandfather said: "The Messenger of Allah (s.w.t) said: 'Whoever gives medical treatment, with no prior knowledge of medicine, is responsible (for any harm done).'" (*Sunan Ibn Majah, Hadith No. 3595*). The outcomes and knowledge derived from the research should be adequate to provide an element of certainty. It should be an indication that the procedure is performed by an authority who has the necessary knowledge and competencies to undertake the intervention.

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