This item was submitted to [Loughborough's Research Repository](#) by the author.
Items in Figshare are protected by copyright, with all rights reserved, unless otherwise indicated.

Terminal sterilization: Conventional methods versus emerging cold atmospheric pressure plasma technology for non-viable biological tissues

PLEASE CITE THE PUBLISHED VERSION

<http://dx.doi.org/10.1002/ppap.201600134>

PUBLISHER

© Wiley-VCH Verlag

VERSION

AM (Accepted Manuscript)

PUBLISHER STATEMENT

This work is made available according to the conditions of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0) licence. Full details of this licence are available at:
<https://creativecommons.org/licenses/by-nc-nd/4.0/>

LICENCE

CC BY-NC-ND 4.0

REPOSITORY RECORD

Marsit, Nagi M., Laura E. Sidney, Matthew J. Branch, Samantha L. Wilson, and Andrew Hopkinson. 2019. "Terminal Sterilization: Conventional Methods Versus Emerging Cold Atmospheric Pressure Plasma Technology for Non-viable Biological Tissues". figshare. <https://hdl.handle.net/2134/23656>.

Terminal sterilization: Conventional methods versus emerging cold atmospheric pressure plasma technology for non-viable biological tissues

Authors

Nagi M. Marsit: Academic Ophthalmology, Division of Clinical Neuroscience, Queen's Medical Centre Campus, University of Nottingham, Nottingham, United Kingdom

Department of Human Tissue, Biotechnology Research Center (BTRC), Libyan Authority for Research, Sciences and Technology, Tripoli, Libya

Laura E. Sidney: Academic Ophthalmology, Division of Clinical Neuroscience, Queen's Medical Centre Campus, University of Nottingham, Nottingham, United Kingdom

Matthew J. Branch: Academic Ophthalmology, Division of Clinical Neuroscience, Queen's Medical Centre Campus, University of Nottingham, Nottingham, United Kingdom

Samantha L. Wilson: Academic Ophthalmology, Division of Clinical Neuroscience, Queen's Medical Centre Campus, University of Nottingham, Nottingham, United Kingdom

Andrew Hopkinson: Academic Ophthalmology, Division of Clinical Neuroscience, Queen's Medical Centre Campus, University of Nottingham, Nottingham, United Kingdom

Corresponding author

E-mail address:andrew.hopkinson@nottingham.ac.uk

Academic Ophthalmology, Division of Clinical Neuroscience, Queen's Medical Centre Campus, University of Nottingham, Nottingham, United Kingdom

Correspondence

Andrew Hopkinson, Academic Ophthalmology, Division of Clinical Neuroscience, Queen's Medical Centre Campus, University of Nottingham, Nottingham, NG7 2UH, United Kingdom.

Email:andrew.hopkinson@nottingham.ac.uk

Abstract

Tissue products are susceptible to microbial contamination from different sources, which may cause disease transmission upon transplantation. Terminal sterilization using gamma radiation, electron-beam, and ethylene oxide protocols are well-established and accepted, however, such methods have known disadvantages associated with compromised tissue integrity, functionality, safety, complex logistics, availability, and cost. Non-thermal (cold) atmospheric pressure plasma (CAP) is an emerging technology that has several biomedical applications including sterilization of tissues, and the potential to surpass current terminal sterilization techniques. This review discusses the limitations of conventional terminal sterilization technologies for biological materials, and highlights the benefits of utilizing CAP.

1 INTRODUCTION

Tissues and biological transplant materials (TBTM), including bone, soft tissues, and other biologically derived biomaterials should be sterilized to prevent transmission of microorganisms to the recipient. TBTM typically possess a natural microbial load/bioburden¹ or acquire one during collection and processing. If not eliminated, this has the potential to cause an infection leading to transplant failure, and further harm to the patient. Prevention of disease transmission is of primary concern to TBTM manufacturers and the regulatory authorities.

Sterilization is the confident and reproducible elimination of all forms of life. Terminal sterilization is considered the final step in the manufacturing process of a sterile product in its final packaging.^[1] Terminal sterilization is used in the processing of TBTM to provide sterility assurance and is generally mandated by national regulatory authorities.^[2] Terminal sterilization is required when: TBTM are processed in non-aseptic conditions; are not treated by any other form of decontamination; use non-sterile consumables; or are stored in conditions that do not prevent microbial growth. There is no ideal sterilization process for all biological materials. Each strategy faces advantages and disadvantages, requiring numerous considerations when choosing sterilization methods, including:

- Material compatibility.
- Reliability against bacterial spores, endotoxins, and viruses.
- Effect on production process.
- Expense.

Although terminal sterilization destroys contaminating microbial agents, the process also devitalizes the cells of the tissue. As a result, terminal sterilization is unsuitable for TBTM that are intended to include viable and healthy donor cells. Non-viable TBTM are routinely used for diverse applications ranging from homotopic, long-term transplants such as bone grafts^[3, 4]; to short-term heterotopic transplants, such as amniotic membrane (AM) which can be used as an ocular surface bandage.^[5, 6] In these situations, terminal sterilization is appropriate. Preservation of the original structure and function of a tissue, both mechanically and biochemically is essential. However, most sterilization methods can substantially damage biological materials.

Classical terminal sterilization methods such as ionizing radiation and ethylene oxide (EtO) have limitations including TBTM degradation, prolonged sterilization cycles, cost, logistical difficulties and inefficiency against viruses, prions, and endotoxins. Thus, an effective sterilization procedure capable of maintaining a balance between sterilization efficacy, cost, and retention of TBTM structural and functional properties is required for elimination of such resistant contaminants.

Trials of non-thermal (cold) atmospheric pressure plasma (CAP) sterilization methods on viable cells and tissues are promising.^[7-11] Although CAP is potentially restricted to the sterilization of thinner TBTM, further optimization could deliver reduced cost, time, logistics, and damage. In contrast with conventional sterilization methods, literature has reported that CAP possesses the ability to eradicate all resistant contaminants such as viruses, prions, endotoxins, and biofilm from the treated surfaces.^[12, 13]

This review compares the limitations of classic terminal sterilization of TBTM including gamma (γ), electron beam (e-beam) and EtO, and addresses the possibility of implementing CAP technologies with a particular focus on the sterilization of non-viable AM.

2 CHALLENGES OF TBTM MANUFACTURING AND RISK OF CONTAMINATION

Tissue processing protocols vary, depending upon tissue structure and composition and the intended application, which determines how well the structural and functional properties of the native tissue need to be maintained. Processing of TBTM may include dissection, intensive, and prolonged washing steps to remove blood and cellular components to diminish the presence of antigens and disease, defatting, demineralization, and decellularization.

TBTM may be preserved dry, or in hydrated form, at ambient or cold storage conditions; they may be aseptically prepared, high level decontaminated, or terminally sterilized.^[14]

Optimized manufacturing procedures are crucial for the quality and safety of the final product.

There are specified international regulatory directives set to ensure prevention of risk from communicable disease transmission agents during procurement, processing, preservation, storage, and use of TBTM (Directive 2004/23/EC).^[15]

In the UK, under Human Tissue Authority (HTA) regulations, viable and non-viable tissues can be prepared without terminal sterilization. However, such procedures require stringent preparation and in-process monitoring compared with terminally sterilized tissues. Long-term

storage of cryopreserved tissue requires specialist storage at -135°C and with specific cryoprotectants such as dimethyl sulfoxide or glycerol; whereas non-viable, dehydrated (freeze-, heat-, or vacuum-dried) tissue can be vacuum-packed and stored at ambient temperature for up to five years.^[16]

In the US, transplantable materials such as bone, tendon, ligament, dura mater, heart valves, skin, cornea, and AM are designated as “human cell, tissue, cellular or tissue-based products” (HCT/P) by the US Food and Drug Administration (FDA), with the stipulation that it is minimally manipulated as regulated under section 361 of the Public Health Service Act (PHSA) and the Code of Federal Regulations (CFR no. 21, Parts 1270 and 1271 of the FDA cGTP). Minimal manipulation is defined as negligible alteration to the tissues’ original biological structure including physical integrity, tensile strength, and elasticity; while allowing for preservation via drying, cryopreservation, and denuding (removal of epithelium).^[17] FDA regulation does not mandate terminal sterilization for HCT/Ps, however, aseptic processing must be used during tissue manufacturing to prevent contamination.^[18]

2.1 Amniotic membrane as an example of a TBTM

AM is a TBTM that has a long history of surgical use, but has varied processing techniques and associated challenges. AM can be used for membrane repair on wound surfaces, or to fill spaces left by non-healing ulcers.^[19-21] AM is commonly used in ophthalmic applications to treat a variety of corneal conditions.^[5] Alongside acting as a transparent, physical shield, AM reportedly possesses protective, antimicrobial, analgesic, and anti-inflammatory properties, that promote wound healing.^[5, 6] Due to its healing properties and low immunogenicity, AM is often applied directly to open wounds.

AM undergoes stringent and tightly regulated processing procedures for clinical application. AM is typically collected from women undergoing preplanned, full-term elective cesarean-sections.^[22] Therefore, donor screening, which involves assessment of information on health and social history, is the first line in disease transmission prevention. Donors must comply with set inclusion criteria, for example test-negative for human immune-deficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), and *Treponema pallidum* (syphilis), among other criteria.^[23, 24]

Under normal health, AM is naturally free of bioburden while in the womb. However, normal flora of the lower genital tract (e.g., gram-positive and gram-negative aerobic and anaerobic

organisms such as genital mycoplasmas and *Streptococcus agalactiae*), are capable of crossing intact membranes to invade the amniotic cavity during labor.[25] However, AM obtained from healthy full-term cesarean sections should have no bioburden. The UK advisory committee on Safety of Blood, Tissues and Organs (SaBTO) guidelines state that: “Estimation of bioburden of skin and amnion is not recommended as the former carries a substantial bioburden and the latter is surgically recovered under aseptic conditions. However, a heavy growth of bacteria from pre-process samples may signify gross contamination and the tissue should not be released unless able to be terminally sterilized by irradiation or other techniques. The potential damage to the integrity of the tissue by the high numbers of bacteria should also be considered before it is used for transplantation.”[26]

Cesarean deliveries do have the potential to introduce some contamination, likely originating from the donor's skin microbial flora, transmitted during AM removal.[27, 28] Other contamination may arise from the operating room environment. Further processing of AM usually takes place in GMP environments subjected to high-level decontamination procedures. AM is generally rendered non-viable during preservation, either by drying or freezing.[29] As a non-viable tissue, currently used surgically, AM is an ideal candidate for terminal sterilization.

3 STERILIZATION OF ABNORMAL BIOLOGICAL CONTAMINANTS

Processing and sterilization protocols are effective for TBTM with low to normal bioburden. Tissues infected with a high bioburden of endotoxin producing, gram-negative bacteria or virulent, antibiotic-resistant bacteria, for example pseudomonas, methicillin-resistant *S. aureus* (MRSA), or *C. difficile*, represent a greater hazard and are unsuitable for transplantation unless a terminal sterilization procedure is used, that is validated for effective removal or complete inactivation of microbial loads.[30] TBTM can also be contaminated by non-living biological agents such as endotoxins, prions, and viruses, which are known to resist most conventional sterilization methods.[31] Most ISO standards exclude viruses and prions from their sterilization validation documents. For example, ISO 14160:2011[32] for liquid chemical sterilization controls risks associated with only bacteria and fungi contamination; however, it is not applicable to TBTM. Also, ISO 11137-1:2006,[33] for validation of radiation sterilization dose does not cover viral contamination and ISO 11135:2014,[34] for validation and control of EtO sterilization methods excludes prion

contamination from its scope. Categorically, these standards indirectly recognize the downsides of industrial sterilization technologies toward particular contaminations. The risk of harvesting and transplanting infected tissue can be reduced, but not eliminated, by specific donor exclusion criteria in the form of detailed medical/social history questionnaires and advanced serological testing. However, terminal sterilization remains the most effective method for eliminating biological contamination hazards associated with donor source, procurement, and manufacturing. Selection of the appropriate sterilization protocol for TBTMs must be considered on a case-by-case basis; considering the possibility of sterilization resistant contaminants.

3.1 Endotoxins

Endotoxins are the lipopolysaccharides (LPS) that make up the outer membranes of the pathogenic and non-pathogenic gram-negative bacteria.[35] Endotoxins present in the blood stream are life-threatening in high doses,[36] due to activation of the immune system causing “endotoxin shock.” Current sterilization technologies only deactivate endotoxin producing bacterial species and are incapable of removing endotoxins themselves. Therefore, there is potential endotoxin existence on sterile products. Endotoxin contamination is of great concern in pharmaceutical and TBTM manufacturing industries, as they are thermostable, resistant to pH change, vary widely in size, and have heterogeneous molecular structures.[37, 38] Aggressive endotoxin removal methods such as high temperatures (250 °C for 30 min, or 180 °C for 3 h)[39] are unsuitable for TBTM. The terminal sterilization radiation doses required to degrade endotoxins are effective only at very high levels,[40] which can be destructive to TBTM. As product removal of endotoxins is more problematic than sterilization; avoiding contamination by employing aseptic technique and current good tissue practice (cGTP) are currently the favored approach.

3.2 Prions

Prions are another challenging form of non-living contamination. They are a pathogenic form of misfolded protein responsible for introducing neurodegenerative disorders such as transmissible spongiform encephalopathies. These potentially fatal prion diseases can be transmitted to healthy patients through contaminated tissue allografts such dura mater and ocular tissue transplants.[41] Prions exhibit a resistance to most known physical and chemical sterilization methods. Even methods combining autoclaving with chemical treatment of

concentrated sodium hydroxide are incapable of completely abolishing prion contamination from reusable hospital devices.[42]

3.3 Biofilm

A biofilm is a complex stratified mass of single or varied genotypes of microbes (bacteria or fungi), compacted to each other and strongly attached to surfaces. Biofilms have high protection capacity against disinfectants and antimicrobials compared to normal microbial form. Thickness and compaction determines microbial biofilm resistance to penetrating oxidative agents. Biofilms are formed on synthetic transplant materials,[43] but are not known to be present on TBTM. However, biofilm presence in water pipes, channels, and surfaces of TBTM manufacturing equipment can be a source of frequent contamination, representing a considerable safety concern. Once these biofilm making microorganisms reach the manufacturing equipment and materials, a reliable sterilization technique is required to eradicate it. Examples of biofilm forming bacteria include: MRSA, *Staphylococcus epidermidis* (*S. epidermidis*), *Staphylococcus aureus* (*S. aureus*), and *Escherichia coli* (*E. coli*).[43]

3.4 Viruses

Non-viable TBTM that have been exposed to chemical treatment, drying or terminally sterilized are less virally infectious than viable tissue preserved at low temperatures.[44] Therefore, transmission of viruses through non-viable TBTM is rare. However, viruses with small, and/or double stranded genomic material have more ability to repair damage to genetic material than viruses with complex genomes,[45] and can resist high radiation doses of 100 kGy.[46]

4 ESTABLISHED STERILIZATION TECHNIQUES FOR TBTM

Challenges of TBTM manufacturing include standardization, maintenance of tissue quality, and sterility, which may ultimately affect clinical outcome. The predominant issue with contemporary terminal sterilization techniques such as γ , e-beam, and EtO, is maintenance of tissue structure and biological properties.[47] However, failure to provide sterile TBTM can result in significant health complications, and cost implications to health care providers.

4.1 Standardization and regulation of sterilization techniques

High temperature sterilization techniques, such as high-pressure steam methods, are unsuitable due to their denaturing and destructive effects on tissue extracellular matrix; they can also coagulate soft tissues[48] and are insufficient for endotoxin inactivation. Other non-thermal, conventional sterilization methods such as EtO, γ , and e-beam are recognized techniques, which are effective when validated correctly.[42] Radiation dosage for sterilization is validated using ISO 11137 (2006), EtO, and pressured steam sterilization are also standardized by ISO 11135 (2014) and ISO 17665-1 (2006)[49] respectively. The achievement of absolute sterility is difficult to determine without destructively testing all batch materials.[50] Therefore, sterile production standards of medical supplies, drugs and TBtMs refer to the sterility assurance level (SAL). SALs are based on the theoretical probability of overkill and demonstration of non-sterility of a particular item following sterilization. SAL 10^{-6} is adopted for medical devices and biological products and is endorsed by most major tissue banking societies and specialized organizations.[51, 52] Using SAL 10^{-6} implies that no more than one item in one million may be non-sterile, or that there is a one in a million chance that an individual microbe will survive sterilization. Nevertheless, the FDA does not specify a particular method of terminal sterilization or a specific SAL for TBtMs. SAL selection is the tissue manufacturer's responsibility and appropriate SALs lower than 10^{-6} can be used if the product is unable to withstand the sterilization process (AAMI ST67 standard). SAL 10^{-3} is used for inanimate medical supplies and have not been reported to be less assured than SAL 10^{-6} products in terms of preventing nosocomial infections. Although current terminal sterilization techniques have revolutionized many industries including medicinal products and tissue supply, higher SALs may come at the cost of damaging TBtM.[53]

4.2 Limitations of current low temperature sterilizations

Current terminal sterilization techniques along with their advantages and disadvantages with respect to TBtM are summarized in Table 1.

269 **Table 1.** Physical and chemical terminal sterilization techniques and their advantages and
270 disadvantages

Technique	Advantages	Disadvantages
Physical		
Pressurized steam (autoclaving)	Inexpensive simple, safe, rapid, and efficient, leaves no toxic residues. [73]	Incompatible with tissues and polymeric biomaterials due to high temperature and moisture that disrupts biochemical structures and causes coagulation of proteins. [42, 168]
	Easy to monitor. [42]	Materials require special permeable packages to ensure steam reaches all surfaces. [42]
	Can sterilize liquids. [42]	
	More effective than dry heat against prions. [42]	
	Used in both industry and clinical settings.	
Ionizing radiation		
Gamma (γ) radiation from ^{60}Co	Effective against spore forming bacteria.	Predominantly only available in industrial and research centers. [42]
	Radiation doses ≤ 25 kGy do not alter the mechanical performance of soft tissues. [169]	High capital cost for installation and maintenance.
	Suitable for heat and moisture sensitive materials.	Expensive ^{60}Co source replenishment. [159]
	Higher penetration (50–80 cm). [45, 170]	Unsuitable for small tissue batch producers.

Technique	Advantages	Disadvantages
	Dose rate approximately 10 kGy/h.	Requires high doses to deactivate viruses (89 kGy).
	Immediate release after processing.	Higher doses than 35 kGy cause tissue damage. [53]
	No need for permeable packaging.	Causes crosslinking and/or peptide chain breakage. [53, 168]
	Leaves no chemical residues or radioactive substances. [168, 171, 172]	Low dose rate (slow dose delivery). [45]
	Cost-effective compared to EtO. [170]	Not appropriate for viral or prion infected tissue. [33]
Electron (e-beam) radiation		High doses required to eliminate endotoxins. [40]
	Can sterilize heat and moisture sensitive materials, and generally more compatible than γ . [42]	High equipment and operational cost. [174]
	Doses up to 34 kGy are less harmful on soft tissues. [173]	Higher doses than 35 kGy damaging to tissues.
	High dose rate (quick sterilization dose delivery within minutes). [45]	High electric consumption. [33]
	No need for permeable packaging.	Not appropriate virally infected human donated tissue grafts. [33]
	Immediate release after processing.	Low penetration depth (5–8 cm). [43, 170]
	No chemical residues or	Not recommended for high density

Technique	Advantages	Disadvantages
Chemical	radioactive substances.[168, 171, 172]	materials.
	Cost effective compared to EtO.[170]	Acceptable sterilization doses are not effective against prions.
Ethylene oxide gas (EtO)		Ineffective against endotoxins.
	Reliable and effective sterilization.[175]	Only available and suitable for large-scale usage.
	Efficient bactericidal, sporicidal, and virucidal activity.[176]	High costs for small scale use.
	Rapidly deactivates hepatitis B and HIV-1 viruses.[177]	Lengthy sterilization process.[168, 178]
	Causes less damage to extracellular matrix than γ , e-beam, and glutaraldehyde methods.[53]	Requires special gas-permeable packaging.[33]
	Suitable for bulk sterilization.	Recognized as a toxic waste by the Environmental Protection Agency (EPA).[60, 168, 178-180]
		Potentially carcinogenic.[60, 181, 182]
		Process monitoring is more complex than radiation, needs to control several parameters.[42, 183]
		Flammable and explosive.[184]

Technique	Advantages	Disadvantages
		Leaves toxic residues on sterilized materials.[168]
		Causes potential damage to tissues.[60, 61, 183, 185]
		Not recommended for sterilization of tissue allografts.[180, 185]
		Danger to facility workers.[186]
		Ineffective against prions.[34]

271

272 Ionizing radiation sterilization at moderate doses is used at large-scale for medical supplies
273 and synthetic prostheses, but there are concerns regarding their destructive effects on TBTMs
274 at higher doses. γ and e-beam radiation are widely applied for tissue sterilization including
275 AM.[[54-57](#)] Twenty-five kGy from both e-beam and γ sources has been internationally
276 accepted as a guaranteed dose, however, the International Atomic Energy Agency (IAEA)
277 standards[[58](#)] recommend a dose of below 25 kGy.[[30](#)] Conversely, concerns regarding viral
278 transmission via allografts from deceased donors potentially infected with HIV/HCV/HBV
279 justify higher doses (e.g., 35 kGy).[[54](#)] Debates regarding optimal sterilization dose reflect
280 concerns regarding unacceptable structural damage or physicochemical changes caused by
281 high radiation doses[[45, 59](#)] and irradiation cost, especially for small tissue manufacturers, is
282 an additional issue.

283 Chemical sterilization, such as EtO, has toxicity concerns due to high oxidative stresses of
284 free radicals and residues, time-consuming processes, expense, and difficult operational
285 requirements. EtO sterilization unavoidably leaves residuals such as ethylene chlorohydrin
286 and ethylene glycol on treated products,[[60](#)] limiting the functionality of biological
287 tissues.[[61](#)] Other chemical sterilization methods, occasionally used for TBTM; are rarely
288 regarded as terminal sterilization due to technical, safety, or biocompatibility barriers. Super
289 critical carbon dioxide (SCCO₂),[[62](#)] characterized by its efficacy against spores, penetration,
290 and biomaterial compatibility,[[62-65](#)] is reported to cause damage to materials, leaves

residues, and is ineffective against endotoxins.[53, 66] Vaporized peracetic acid (PAA) gas plasma, has been proven to have broad germicidal action over short-time periods,[67] and is compatible with most collagenous materials and tissues.[68-70] However, PAA has time and cost constraints[71] and additionally, PAA sterilized ophthalmic instruments have been documented to cause serious ophthalmic and skin damage with contact, leading to withdrawal from the market place.[64, 72, 73] Similarly, vaporized hydrogen peroxide (H₂O₂) gas plasma is used efficiently for TBTM sterilization and is FDA approved.[74, 75] However, it has problems regarding adverse reactions with the functional properties of the tissue and medical materials.[76, 77] Glutaraldehyde sterilization protocols are relatively inexpensive, effective against most bacteria and viruses, but limited by long process cycles and toxicity to recipient tissues and potentially crosslinking effects.[64]

5 COLD ATMOSPHERIC PRESSURE GAS PLASMA FOR TERMINAL STERILIZATION

Plasma³ has been widely investigated for medical applications in recent years. Progressive findings regarding the role of plasma in the deactivation and elimination of biological contamination demonstrates the potential for this technology to overcome the drawbacks of conventional sterilization methods of heat sensitive materials including TBTM.

5.1 Thermal and non-thermal plasmas

Plasmas at atmospheric pressure can be classified in terms of temperature into two categories, thermal[79, 80] and non-thermal.[81-83] In thermal plasma, the charged particles, neutral electrons, and heavy particles all have the same high temperatures (in thermodynamic equilibrium with the surrounding temperature) and are almost fully ionized; while, in the non-thermal plasma the temperature of gas, atoms, and molecules remains low[84] because of the slight ionization of the used gas,[79] with only electrons at high temperature. Due to this variation of the constituent's temperature, non-thermal plasma is also termed non-equilibrium plasma.[85, 86]

5.2 Low and atmospheric pressure plasmas

Given that thermal plasma produces high gas temperature, non-thermal “cold” plasma is much more suitable as an emerging sterilization method,[[80, 85](#)] for inactivation of microbial loads on human tissues and heat sensitive surfaces.[[87](#)] Furthermore, cold plasma can be produced at low pressures, under vacuum, but for practicality and economic reasons, it is more convenient and cost-effective when generated at atmospheric pressure and therefore called cold atmospheric-pressure plasma (CAP).[[86](#)]

CAP is obtained by exposing gas flow (either air, or noble gases such as oxygen, nitrogen, argon, or helium) to a high electric field which partially ionizes the gas atoms producing a sustained plasma. This plasma contains a collection of excited electrons, negative and positive ions, excited gas species, for example, O, O_2^+ , O_3 , OH^+ , reactive oxygen species (ROS), NO and NO_2 reactive nitrogen species (RNS), free radicals, and UV-photons at different wavelengths.[[88](#)] These nontoxic gases become germicidal only after the plasma is ignited, since they are not biocidal on their own.[[89](#)] Concentration of produced plasma agents (i.e., ROS, RNS, UV, free radicals, charged particles) depends on the operation parameters of the plasma source; namely loaded gas, gas pressure, flow rate, electric voltage, etc.

5.3 CAP systems

CAP can be provided by three different systems (Figure 1): (i) direct plasma, known as the dielectric barrier discharge (DBD) system. By design, the DBD system safely uses the material to be sterilized as a grounded electrode, which the current flows through, while the other electrode is connected to a high voltage; air is utilized as the operating gas, and the distance between plasma source tip and the object is a few millimeters[[79](#)]; (ii) “indirect plasma,” also known as atmospheric pressure plasma jet, which is deployed by a plasma needle/pen (narrow focused jet) or plasma torch systems which have broader streams and cover larger surface areas.[[90](#)] These devices generate plasma between two electrodes, transferred through a gas flow to the object to be treated, the distance between the object and the device ranges from millimeters to centimeters. The reactive species are generated by igniting plasma in an operating gas such as air, or by helium or argon plasmas in an admixture of oxygen or nitrogen[[91](#)]; (iii) hybrid systems or coronal discharge, have characteristics of both direct and indirect plasmas.[[79, 92](#)]

Figure 1. Schematic diagram showing non-thermal, cold atmospheric pressure plasma system types

5.4 Mechanisms of microbial inactivation by CAP

CAP technologies have been used effectively to eliminate microorganisms on living tissues in several clinical applications,[8, 79, 93-100] including inactivation and eradication of fungi, and vegetative and spore-forming bacteria.[85, 88, 101] The microbial inactivation effect of CAP can be attained by direct exposure to both the ignited plasma discharge products such as ROS, RNS, UV radiation, or indirectly through the long-lived species that are capable to reach the treated substrate without the electric field effect.[90] Generally, decontamination through plasma treatment is accomplished via oxidative stress arisen from synergetic actions of plasma discharge products.[87, 102]

The specific plasma agent responsible for the mechanism of CAP killing is not clearly corroborated in literature[7, 88]; although CAP is proven to be damaging to bacterial cell walls, primarily due to ROS and RNS.[103] These charged particles have sufficient ability to induce high oxidative stress which cause damage in microbial cells via fast direct interactions.[80] It has been postulated that the accumulation of plasma charged particles over the bacterial cell membrane causes membrane rupture through electrostatic disruption[104]; or that the reactive species permeabilize and penetrate the cell walls before reacting with DNA via complex mechanisms.[105] Membrane damage through lipid peroxidation is another major cause of bacterial death by CAP. The effect by heat and UV is argued to be indirect or negligible.[106, 107] However, CAP's microbicidal action produced

by various plasma sources are reported to target viable cellular components such cell membrane, protein, and DNA. The effect of CAP is believed overwhelming the DNA repair mechanisms of the bacterial cells.[7]

5.5 Effects of CAP on vegetative and spore-forming bacteria

Plasma agents destroy different microbial entities irrespective of their molecular defense mechanisms. Examples reported of CAP capability for decontaminating multidrug resistant bacteria including the highly resistant MRSA[108-110] and *Pseudomonas aeruginosa*. [109] Notably, CAP is also effective on the sterilization resistant *Deinococcus radiodurans* (*D. radiodurans*) bacteria.[111] Less resistant vegetative bacteria have also been tested against the antimicrobial activity of CAP, and were eliminated with different degrees of survival, including gram-negative: *E. coli*, [110, 112, 113] *Salmonella typhimurium*, [114] and gram-positive *S. epidermidis*, [89, 112, 115] *S. aureus*, [89, 113] *Micrococcus luteus*, [94] *Streptococcus pyogenes*, [89] *Enterococcus faecalis* (*E. faecalis*), [116] and *Enterococcus faecium*. [89] Gram-negative bacteria are more susceptible to gas plasma treatments than gram-positive [103, 117] and differences in susceptibility are thought to be due to variation in the thickness of the peptidoglycan murein layer in the bacterial cell wall. [85, 103]

Skin floral bacteria *S. epidermidis* is of particular importance in sterilization of TBTM given its frequent association with contamination from procurement and processing sites. It is normally found in the hair follicle where it is protected from antiseptics. CAP penetration has the capacity to reach deep into hair follicles [118] and disinfect bacteria by 94%. [119] Gram-positive skin flora *Propionibacterium acnes* (*P. acnes*), reported to cause post-transplantation and implantation infection, are also effectively sterilized by CAP even in protected aggregated forms. [120]

Spore-forming bacteria are typically resistant to many established sterilization protocols, and are often used as a model organism for sterilization verification. Studies have demonstrated CAP efficacy against bacterial spores, including: *Bacillus subtilis* (*B. subtilis*), *C. difficile*, *Bacillus atrophaeus* (*B. atrophaeus*), *Bacillus safensis* (*B. safensis*), *Bacillus megaterium* (*B. megaterium*), *B. megaterium* 2c1, and *Bacillus thuringiensis* (*B. thuringiensis*) E24. [121, 122] Studies have shown CAP has effective sporicidal action even in humid conditions, [123, 124] when spores are stacked together or covered by debris.

5.6 Effect of CAP on abnormal contamination

TBTM manufactured in a sterile environment using cGTP protocols are unlikely to have resistant contamination such as endotoxins, prions, viruses, and biofilms unless a pre-processing infection has occurred. Efficient sterilization should be able to inactivate all forms of disease causing contamination. The advantage of CAP sterilization compared to traditional methods is its powerful efficacy to eliminate resistant contamination and removal through its etching action, which is highly dependent upon applied plasma source. For instance, plasma jets have more etching capabilities than DBD systems. The plasma density, gas mixture, and radical content are important parameters in etching of protein residues from treated surface by chemical degradation and volatilization mechanisms.[125] CAP has been demonstrated to be effective for inactivation of LPS endotoxin removal from treated surfaces within minutes.[126, 127] Similarly, it has been shown that CAP is efficient in removing amyloid fibril aggregates (protein structure mimics prion) from a surfaces, and that aggregates outside the plasma diameter were degraded, while those within the plasma focus were consistently removed.[128] The use of a CAP system with a negative corona discharge has been shown to have a significant effect on prions and may reduce the infectivity of prion particles by several orders of magnitude.[129] This was believed to be mediated by the generated reactive particles. Additionally in this study, the source of CAP had different effects on the viability of brain cells; a positive streamer discharge killed the cells, whereas point-to-point, cometary, and negative corona discharges did not result in a loss of cell viability. This indicates that the discharge configuration is an important parameter to consider when sterilizing viable tissues with CAP.

TBTM contaminants such as the anaerobic gram-positive *P. acnes* and *Staphylococcus* have been proven to form in vivo and in vitro biofilms, and develop resistance to gentamicin-loaded implants for orthopedic surgery,[43] causing biomaterial/prosthesis transplant infection and failure.[130] Biofilms of *P. acnes* bacteria have been found to be considerably inactivated by two types of plasma jet over short-time periods.[120] Biofilms of MRSA, *S. epidermidis*, *S. aureus*, and *E. coli* are also removed by CAP treatment.[12] Similarly, CAP have efficiently removed biofilms of antifungal resistant *Candida albicans* (*C. albicans*).[131] This effect can potentially be enhanced by adding oxygen to the plasma discharge.[132] Studies have shown that viruses can be eliminated by CAP, due to the destruction of the protein coat, rather than a direct effect on viral DNA.[133]

Several factors may affect the dose or the exposure time required to achieve sterilization. These factors are related to the plasma device operational conditions or the microorganism conditions before and after exposure, e.g., bacterial species, bacterial culture age (growth phase), bacterial medium during, and post-treatment.[134] The eradicating effect of CAP on various microorganisms is well-established in literature,[90, 129] however, studies on sterilization and removal of biological non-living disease causing agents would have a promising medical applications.[13, 129] However, CAP system variation, the flexibility of utilizing variable operational conditions along with the different applications have resulted in complication when comparing the literature findings. Table 2 shows examples of the sensitivity of microorganisms of medical importance and other biological contaminants resistant to sterilization, treated with different CAP devices under various experimental conditions, with differences in exposure times and contamination reductions. CAP device specifications and the applied dose were omitted due to the aforementioned plasma delivery complexities. Often, the time required to inactivate or sterilize the microbial/biological contaminations is much shorter than those applied in other established sterilization methods regardless of the CAP system used. To achieve SAL 10^{-6} sterilization, exposure duration (plasma dose) may be extended. Therefore, it is important to have information on the level of initial material contamination if CAP is chosen as a sterilization protocol. It can be difficult to contrast and compare CAP efficacy on biological contamination due to the variability in CAP parameters and systems; however, this does not indicate that CAP is ineffective.

Table 2. Examples of susceptibility of vegetative bacteria, fungi, bacterial spores, endotoxins, prions, and biofilm to CAP treatment

Microorganism	Importance	Exposure substrate	Log reduction or % sterilization	Exposure time (s)	Ref
aKCTC, Korean Collection for Type Cultures, Korea. bATCC, American Type Culture Collection, USA. cDSM, Leibnitz Institute DSMZ-German Collection of Microorganism and Cell Cultures, Germany. dNA, not available.					
Vegetative bacteria (gram-negative)					
<i>E. coli</i>	Clinical pathogen	Agar medium plates	5 log	600	[<u>12</u> <u>2</u>]
<i>E. coli</i>	Clinical pathogen	Glass slides	100%	1	[<u>18</u> <u>7</u>]
<i>E. coli</i> KCTC _a 1039	Clinical pathogen	Thin glass covers	10 log	7	[<u>12</u> <u>1</u>]
			100%	60	
<i>E. coli</i> O157:H7 (C9490)	Foodborne pathogens	Dry almonds	1.34 log	20	[<u>18</u> <u>8</u>]
<i>E. coli</i> O157:H7 (ATCC _b 35150)					
<i>E. coli</i> O157:H7 (ATCC 43894)					
<i>Salmonella anatum</i> F4317					

Microorganism	Importance	Exposure substrate	Log reduction or % sterilization	Exposure time (s)	Ref
<i>Salmonella stanley</i> H0558					
<i>Salmonella enteritidis</i> PT30					
Vegetative bacteria (gram-positive)					
<i>P. acnes</i> KCTC 3314	Skin flora	Coated glass slides	7 log	600	[120]
<i>D. radiodurans</i>	Radiation, drying, and oxidizing agent resistant	Aluminum discs	3 log	1800	[122]
<i>Lactobacillus acidophilus</i>	Oral caries producing bacteria	Hydroxyapatite	1.5–2 log	6	[189]
<i>Streptococcus mutans</i>					
<i>Listeria innocua</i> (ATCC 33090)	Non-pathogenic surrogate for the foodborne pathogen <i>monocytogenes</i>	Chicken meat and skin	3.3 log	480	[150]
Fungi					
<i>C. albicans</i> (thickness of 10–20 mm)	Pathogenic fungus	Polystyrene wafers	95%	300	[132]

Microorganism	Importance	Exposure substrate	Log reduction or % sterilization	Exposure time (s)	Ref
<i>C. albicans</i>	Antifungal resistant (fluconazole-resistance)	Air	>90%	600	<u>[190]</u>
<i>Candida krusei</i>		Water	>90%	60	
<i>Candida glabrata</i>					
<i>Aspergillus flavus</i> (ATCC 327)	Mycotoxin producing food contaminants	Hazelnuts	4.50 log	300	<u>[191]</u>
<i>Aspergillus parasiticus</i> (ATCC 1041)			4.19 log		
<i>Aspergillus parasiticus</i> 798 TUBITAK-MAM	Bio-indicator fungus	Vegetable and legumes seed surfaces	3 log	900	<u>[192]</u>
<i>Penicillium</i> MS1982					
Spore-forming bacteria					
<i>B. subtilis</i>	Sterilization resistant	Thin glass covers	10 log	24	<u>[121]</u>
			100%	120	

Microorganism	Importance	Exposure substrate	Log reduction or % sterilization	Exposure time (s)	Ref
<i>B. safensis</i> , DSMc19 292T	Sterilization resistant	Aluminum discs	>6 log	3600	[122]
<i>B. megaterium</i> , ATCC 14581T			100%	5400	
<i>B. megaterium</i> DSM 30587 (2c1)					
<i>B. atrophaeus</i> DSM675	Sterilization resistant	Aluminum discs	>3 log	5400	[122]
<i>B. thuringiensis</i> DSM 30879 (E24)					
<i>B. subtilis</i>	Sterilization resistant	Glass slide and aluminum substrates	4 log (He plasma)	<600	[193]
			8 log (air plasma)		
<i>B. atrophaeus</i>	Biological indicator for thermal sterilization (heat resistant)	Commercial spore strip	≥ 6 log 10	60	[124]

Microorganism	Importance	Exposure substrate	Log reduction or % sterilization	Exposure time (s)	Ref
Endotoxins					
LPS from <i>E. Coli</i> ATCC 8739	Pyrogen	Glass slides	100%	10	[187]
Viruses					
Adenovirus, non-enveloped double stranded DNA virus	Human infectious disease causing	PBS solution	6 log	240	[13]
Bacteriophage lambda (λ phage)	Virus that infects bacteria	Buffer	6 log	20	[133]
Bacteriophage lambda (λ phage) C-17 (ATCC 23724-B1)	Virus that infects bacteria	NA _d	4–6 log	600	[194]
Lytic bacteriophage (rambo; microphage)					
MS2 bacteriophage ATTC 15597-B1	Surrogate of human enteric viruses such as norovirus that causes infectious gastroenteritis	Phage suspension	4.98–7.06 log	450	[195]
Influenza virus type A (H5N2)	Airborne respiratory	Viral aerosol	4 log (99.20)	180	[196]

Microorganism	Importance	Exposure substrate	Log reduction or % sterilization	Exposure time (s)	Ref
	pathogen	suspension	%)		
Human parainfluenza virus type 3 strain C-243 ATCC VR-93			6.5 log (99.22 %)		
Respiratory syncytial virus-A ATCC VR-26			3.8 log (99.00 %)		
Prions					
Scrapie (Rocky Mountain Laboratory strain, RML5)	Surrogate of human prion	1% mouse brain in PBS solution	100%	600–1200	[129]
Biofilm					
<i>P. aeruginosa</i> SG81	Clinical pathogen	Polycarbonate discs.	4.83 log	300	[117]
			7.11 log	600	
<i>S. epidermidis</i> RP62 A	Skin flora	Polycarbonate discs	2.77 log	300	[117]
			3.38 log	600	

Microorganism	Importance	Exposure substrate	Log reduction or % sterilization	Exposure time (s)	Ref
<i>Salmonella enterica serovar typhimurium</i>	Clinical pathogens	Lettuce	5 log	300	[197]
<i>Listeria monocytogenes</i>					
<i>E. coli</i>					
<i>E. faecalis</i>					
<i>C. albicans</i>	Clinical pathogen	Inanimate surface	6 log	240	[131]

466

467 5.7 Use of CAP for TBTM sterilization

468 CAP has been evaluated as a safe and efficient procedure for decontamination of skin wounds,
469 ulcers, and infected tissues in patients, and there are commercially available products such as
470 the kINPen[135] and the DBD plasma generator (PlasmaDerm® VU-2010).[136] Reports
471 often emphasize the biocompatibility of plasma treatment on viable cells and tissues,
472 including ocular surface tissues.[100, 137-139] These effects are deleterious to microbial
473 contamination, but have thus far not been proved to induce necrotic, apoptotic, or
474 morphological changes in surrounding tissues. Furthermore, no significant effects on living
475 cell viability were reported.[110] In other studies, a slight reduction in viability through
476 necrosis of in vitro culture of mucosal cells was observed, however, no mutagenic effects
477 were observed.[135, 140] The reason CAP mechanisms are generally harmless to human cells
478 and tissue is attributed to CAP's superficial penetration,[126, 141] and potentially that
479 multicellular eukaryotic tissues have more complicated mechanisms to enable survival of
480 oxidative stresses introduced by plasma agents, than prokaryotic cells.[142] Limited

penetration could be an obstacle to CAP sterilization of TBTM with thick, heterogeneous size, and architecture such as bone graft materials.[141] However, dried, thin, soft tissues such as skin, facia, dura mater, AM, tendons, and laminate of cartilage and bone are all candidates for CAP sterilization.[143] The defined advantages and disadvantages of CAP sterilization of TBTM are listed in Table 3.

Table 3. Advantages and disadvantages of CAP sterilization of TBTM

Advantages	Disadvantages
Biocompatible with viable and non-viable tissues.	Methods not yet validated.
No toxic chemical residue left on treated object.[135]	Low penetration power so may be not suitable for thick TBTM materials.[141]
Shorter exposure time than established sterilization methods (seconds to minutes).	Difficult to apply to packaged materials.
No toxic effects to operators and the environment.[198]	Not validated as terminal sterilization that offers SAL of 10^{-6} .
Can remove bacterial cells and viruses from sterilized surfaces.	Many parameters (e.g., loaded gas, gas pressure, flow rate, voltage, exposure time, and sample distance) need to be controlled to get the desired capacity of charged species.
Effective on endotoxins, prions and bacterial, and fungal biofilms.[131]	
Delivers uniform treatment to uneven surfaces of biological materials.[199]	
CAP gas capable of reaching confined and narrow spaces.[81]	
Microorganism resistance to CAP is unlikely to	

Advantages	Disadvantages
occur.[105]	
Inexpensive.[200]	
Can be used portably or in smaller scale (such as in laminar flow hoods and isolators).[200]	

488

489 5.8 CAP as a potential technique for thin tissue sterilization

490 At the time of this review, there were no studies available evaluating CAP for sterilization of
491 non-viable TBTM. However, if we consider non-viable AM as an example, a number of
492 factors should be considered when optimizing CAP specifically, tissue thickness, treatment
493 area, surface morphology, probable type and count of contamination, and whether
494 sterilization will occur before or after packaging.

495 A reliable sterilization method must have sufficient penetration capability. Studies have
496 demonstrated that CAP delivers ROS in the range of 150–1500 μm [[144](#)] when employed on a
497 tissue-equivalent material and at over 5000 μm for agarose gels.[[100](#)] For intact viable skin,
498 reactive species can penetrate up to 10 μm depth.[[135](#)] The penetration of H_2O_2 produced by
499 CAP into euthanized rat skin and chicken breasts was shown to go up to 4000 μm . [[145](#)]
500 Furthermore, experiments on polyester fabric materials assert that the distance from plasma
501 nozzle to substrate, exposure time, and thickness of substrate, have an effect on plasma
502 penetration, yet suggests longer exposure time renders a sufficient amount of reactive species
503 accumulating on one side to diffuse to the other side of the porous material.[[146, 147](#)]
504 Moreover, it has been demonstrated that nitric oxide (NO) generated by topical application of
505 DBD over a human skin and reconstructed epidermis were safe on living tissue and able to
506 penetrate and cause changes in microcirculation up to 6000–8000 μm on treated skin
507 areas.[[148](#)] Dried AM with a thickness of approximately 20 μm [[149](#)] will therefore lie within
508 the penetration range of CAP and should not require lengthy exposure times.
509 Surface topography of treated tissue present challenges in sterilization, as changes can occur
510 during chemical or mechanical processing, creating rough surfaces and microgrooves where
511 microorganisms can reside and proliferate. Tissue surface irregularity enables contaminant

bacteria to migrate from the surface into the tissue, protecting it from the biocidal effect of sterilization.[150] There are natural intercellular microholes on AM epithelial surface (Figure 2A and B), which have been proven to allow gas transmission through dried and cryopreserved AM upon transplantation.[151, 152] These microholes are impermeable to bacteria such as *E. coli*, *Pseudomonas*, *Klebsiella*, and *Staphylococcus*. [153] CAP can easily reach narrow, confined spaces, and microgrooves on surfaces.[81] and mobility of plasma gas can allow for treatment of microspaces.[122, 154] Recent studies reported CAP efficacy in reducing microbial contamination adhered to rough surfaces of chicken skin,[150] titanium implant surfaces,[155] and root canals, especially in dry state conditions.[156] This supports the appropriate use of CAP for sterilization of dry AM with a comparably soft homogenous surface (Figure 2A and C).

Figure 2. Scanning electron microscopy image of dried AM (A and B – epithelial side; C and D – stromal side). (A) Intact polygonal epithelial surface cells with occasional intercellular spaces (scale bar: 10 µm). (B) Box in (A) magnified to show distinct natural intracellular microholes (white circles) around the cell (scale bar: 1 µm). (C) Smooth regular stromal surface of AM (scale bar: 10 µm). (D) Collagen fibrils on the stromal side with tiny microgrooves (white arrows), scale bar: 1 µm)

Additionally, CAP treatment of large tissues requires a plasma source capable of delivering plasma components over wider surface areas. Single CAP jets are limited to a few

millimeters, for example, 25 mm²,[\[157\]](#) thus are unsuitable, but micro-discharge plasma devices have been used effectively for biofilm treatment on a 177 cm² surface area.[\[131\]](#) Plasma torches are able to treat areas of approximately 25 cm² and DBD and jet torches appear to be favorable for large size membranous grafts[\[81\]](#) and have potential to be developed to operate as a systemic scanning system for tissue materials with large surface area. The area of AM grafts are generally 4–100 cm², thus CAP systems could be developed to accommodate this.

There are parameters related to the plasma system operational conditions that will affect use, such as: the voltage, loaded gas, gas pressure, flow rate, exposure time, and sample distance from plasma nozzle.[\[158, 159\]](#) The interplay of these parameters could yield sufficient plasma density and composition, or conversely might change the treatment outcome; causing inconsistency in sterilization cycles.[\[160\]](#) For instance, operational parameters such as ion and UV flux, electric field, and gas flow might not have direct influence on the antibacterial efficiency, while other factors related to the method and conditions of application such as distance from the plasma nozzle and exposure time have a distinct influence on treatment efficiency.[\[161\]](#)

An effective treatment that causes no damage to tissues requires a highly standardized, balanced, and homogenous current discharge,[\[162\]](#) which can be attained by adjusting the circuit, gas flow, and power supply parameters.[\[87\]](#) As varied modalities of CAP systems have been used as decontamination tools on different biological substrates, such as human skin and food products, it is possible to develop a CAP device that copes with thin non-viable membranous tissue sealed in sterile packaging.

To maintain sterility of a manufactured TBTM, CAP should be applied after packaging or in-package and sealed in a sterile environment. Use of CAP for in-package sterilization has been tested effective against spores, used to decontaminate foods, and is compatible with some packaging materials.[\[124, 163\]](#) DBD plasma configurations developed with efficient sporicidal actions were found to safely fit several shapes of Tyvek packaging materials used for sterile wrapping of medical instruments.[\[164\]](#) Different packaging materials including polyethylene, polypropylene, and nylon loaded with microbial pathogens have shown no change in the physical properties after treatment with low pressure plasma.[\[165\]](#) Recent studies have shown that generating plasma inside a closed environment can prevent post-packaging contamination of sterilized products.[\[166\]](#)

Another attractive advantage of CAP over conventional sterilization is cost-efficiency. Cold plasma generators can be scaled-down as portable devices in a regular laboratory instrument

size, for use on the bench, which suits application in small-scale tissue production.[8] Close proximity to tissue preparation site can potentially minimize cost of logistics and are not as complex as performing terminal sterilization away from the production site.

Direct or indirect CAP systems may be appropriate for AM sterilization, as they can be operated at atmospheric pressure and at nearly ambient temperature,[167] can deliver large quantities of active species with sufficient penetration power of plasma agents,[80] and can treat reasonably large areas inside the final product packaging. Small mobile handled CAP devices could be an economical choice for AM sterilization inside the sterile area or alternately, an on-bench contained chamber design for in-package sterilization may be more applicable.

6 CONCLUSION

Current terminal sterilization methods such as EtO, ionizing radiation, and chemical sterilization methods have several disadvantages including toxicity, high running-costs, and inefficacy against abnormal contamination. CAP is a terminal sterilization technique that is applicable to living tissues without known harm or side effects, that has been proven to destroy both normal and abnormal contamination. CAP is inexpensive but limited by tissue thickness, post-packaging penetration, and reproducibility. Choice of CAP for TBTM sterilization should be done on individual basis, dependent on tissue characteristics, manufacturing protocol, and intended use. However, if CAP can be adapted for TBTM, it holds a vast amount of promise.

ACKNOWLEDGMENTS

The authors alone are responsible for the content and writing of the manuscript. Funding from The Authority for Research, Science, and Technology of the Ministry of Higher Education and Scientific Research-Libya (Scholarship 404/2013) is gratefully acknowledged.

594
595
596
597
598
599
600
601
602
603
604
605
606
607
608
609
610
611
612
613
614
615
616
617
618
619
620
621
622
623
624
625
626
627

REFERENCES

1
B. J. Lambert, T. A. Mendelson, M. D. Craven, AAPS Pharm. Sci. Tech. 2011, 12, 1116.
CrossRef | Web of Science® Times Cited: 13
2
D. Hussong, AAPS Pharm. Sci. Tech. 2010, 11, 1482.
CrossRef | Web of Science®
3
S. Stevenson, Orthop. Clin. North. Am. 1999, 30, 543.
CrossRef | PubMed | CAS | Web of Science® Times Cited: 117
4
T. Boyce, J. Edwards, N. Scarborough, Orthop. Clin. North. Am. 1999, 30, 571.
CrossRef | PubMed | CAS | Web of Science® Times Cited: 170
5
H. S. Dua, J. A. Gomes, A. J. King, V. S. Maharajan, Surv. Ophthalmol. 2004, 49, 51.
CrossRef | PubMed | Web of Science® Times Cited: 305
6
F. Gindraux, R. Laurent, L. Nicod, B. de Billy, C. Meyer, N. Zwetyenga, L. Wajszczak, P.
Garbuio, L. Obert, Recent Pat. Regen. Med. 2013, 3, 193.
7
J.-W. Lackmann, J. E. Bandow, Appl. Microbiol. Biotechnol. 2014, 98, 6205.
CrossRef | PubMed | CAS | Web of Science® Times Cited: 14
8
P. Brun, M. Vono, P. Venier, E. Tarricone, V. Deligianni, E. Martines, M. Zuin, S. Spagnolo,
R. Cavazzana, R. Cardin, I. Castagliuolo, A. L. Valerio, A. Leonardi, PLoS ONE 2012, 7, 14.
CrossRef | Web of Science® Times Cited: 32 | ADS
9
C. Hoffmann, C. Berganza, J. Zhang, Med. Gas Res. 2013, 3, 21.
CrossRef | PubMed
10
C. Ulrich, F. Kluschke, A. Patzelt, S. Vandersee, V. A. Czaika, H. Richter, A. Bob, J. Hutten,
C. Painsi, R. Huge, A. Kramer, O. Assadian, J. Lademann, B. Lange-Asschenfeldt, J. Wound
Care 2015, 24, 198.

628 CrossRef
629 11
630 R. Laurita, F. Alviano, C. Marchionni, P. M. Abruzzo, A. Bolotta, L. Bonsi, V. Colombo, M.
631 Gherardi, A. Liguori, F. Ricci, M. Rossi, A. Stancampiano, P. L. Tazzari, M. Marini, J. Phys.
632 D 2016, 49, 364003.
633 CrossRef | Web of Science® | ADS
634 12
635 M. Hee Lee, B. Joo Park, S. Chang Jin, D. Kim, I. Han, J. Kim, S. O. Hyun, K.-H. Chung, J.-
636 C. Park, New J. Phys. 2009, 11, 115022.
637 CrossRef | Web of Science® Times Cited: 28 | ADS
638 13
639 J. L. Zimmermann, K. Dumler, T. Shimizu, G. Morfill, A. Wolf, V. Boxhammer, J. Schlegel,
640 B. Gansbacher, M. Anton, J. Phys. D 2011, 44, 505201.
641 CrossRef | CAS | Web of Science® Times Cited: 33 | ADS
642 14
643 J. Komender, Ann. Transplant. 2004, 9, 88.
644 PubMed
645 15
646 Council of Europe, Guide to Safety and Quality Assurance for Organs, Tissues and Cells, 2nd
647 ed., Council of Europe Publishing, Strasbourg, Belgium 2004.
648 16
649 H. Gillan, K. Bennett, P. Yates, Review of Long-Term Storage of Tissue Products, N.B.a.
650 Trnasplant, Editor. 2010, NHS Blood and Transplant: UK.
651 17
652 F. D. A. U.S. Department of Health and Human Services, Minimal Manipulation of Human
653 Cells, Tissues, and Cellular and Tissue-Based Products – Draft Guidance for Industry and
654 Food and Drug Administration Staff. FDA, New Hampshire Avenue, Silver Spring, USA
655 2014.
656 18
657 S. Kuroda, A. S. Viridi, Y. Dai, S. Shott, D. R. Sumner, Calcif. Tissue Int. 2005, 77, 212.
658 CrossRef | PubMed | CAS | Web of Science® Times Cited: 30
659 19
660 I. Mermet, N. Pottier, J. M. Sainthillier, C. Malugani, S. Cairey-Remonnay, S. Maddens, D.
661 Riethmuller, P. Tiberghien, P. Humbert, F. Aubin, Wound Repair Regen. 2007, 15, 459.

662 Wiley Online Library | PubMed | Web of Science® Times Cited: 67
 663 20
 664 F. E. Kruse, K. Rohrschneider, H. E. Völcker, *Ophthalmology* 1999, 106, 1504.
 665 CrossRef | PubMed | CAS | Web of Science® Times Cited: 180
 666 21
 667 M. T. Rodríguez-Ares, R. Touriño, M. J. López-Valladares, F. Gude, *Cornea* 2004, 23, 577.
 668 CrossRef | PubMed | Web of Science® Times Cited: 53
 669 22
 670 P. J. Addis, C. Hunt, S. Hartley, *Br. J. Ophthalmol.* 2001, 85, 228.
 671 CrossRef | PubMed | CAS | Web of Science® Times Cited: 19
 672 23
 673 Current Good Tissue Practice, American Association of Tissue Banks, McLean, Virginia.
 674 2006.
 675 24
 676 International Standards for Tissue Banks, World Scientific, Singapore. 2003.
 677 25
 678 C. A. Combs, T. J. Garite, J. A. Lapidus, J. P. Lapointe, M. Gravett, J. Rael, E. Amon, J. K.
 679 Baxter, K. Brady, W. Clewell, *Am. J. Obstet. Gynecol.* 2015, 212, 482.
 680 PubMed
 681 26
 682 SaBTO, Retrieval of Material for Donation Testing. Infectious Diseases and Blood Policy,
 683 UK 2011.
 684 27
 685 S. Hill, *AORN J.* 2008, 88, 731.
 686 CrossRef | PubMed
 687 28
 688 H. R. Aghayan, P. Goodarzi, A. Baradaran-Rafii, B. Larijani, L. Moradabadi, F. Rahim, B.
 689 Arjmand, *Cell Tissue Bank* 2013, 14, 401.
 690 CrossRef | PubMed | Web of Science® Times Cited: 2
 691 29
 692 A. Hopkinson, R. McIntosh, P. Tighe, D. James, H. S. Dua, *Invest. Ophthalmol. Vis. Sci.*
 693 2006, 47, 4316.
 694 CrossRef | PubMed | Web of Science® Times Cited: 57
 695 30

696 J. Morales Pedraza, A. Lobo Gajiwala, M. E. Martinez Pardo, *Cell Tissue Bank* 2012, 13, 15.
697 CrossRef | PubMed | CAS | Web of Science® Times Cited: 1
698 31

699 N. Yusof, A. Hassan, A. R. Shamsudin, A. C. Yong, M. N. F. A. Rahman, H. Mohamad,
700 Sterilisation of Tissues Using Ionising Radiations (Eds.: J. F. Kennedy, G. O. Phillips, P. A.
701 Williams), Woodhead Publishing Limited, Abington, Cambridge, England 2005, p. 319.
702 CrossRef
703 32

704 ISO-14160, Sterilization of health care products – Liquid chemical sterilizing agents for
705 single-use medical devices utilizing animal tissues and their derivatives – Requirements for
706 characterization, development, validation and routine control of a sterilization process for
707 medical devices, in The International Organization for Standardization. 2011 Geneva,
708 Switzerland.
709 33

710 ISO-11137-1, Sterilization of health care products, Radiation, Part 1, Requirements for
711 development, validation and routine control of a sterilization process for medical devices, in
712 International Organization for Standardization. 2006: Geneva, Swetzerland.
713 34

714 ISO-11135, Sterilization of health care products – Ethylene Oxide – Requirements for
715 development, validation, and routine control of a sterilization process for medical devices, in
716 International Organization for Standardization. 2014: Geneva, Switzerland.
717 35

718 G. Ramachandran, *Virulence* 2014, 5, 213.
719 CrossRef | PubMed | Web of Science® Times Cited: 27
720 36

721 N. Mamalis, H. F. Edelhauser, D. G. Dawson, J. Chew, R. M. LeBoyer, L. Werner, J.
722 Cataract Refract. Surg. 2006, 32, 324.
723 CrossRef | PubMed | Web of Science® Times Cited: 116
724 37

725 E. T. Palva, P. H. Makela, *Eur. J. Biochem.* 1980, 107, 137.
726 Wiley Online Library | PubMed | CAS | Web of Science® Times Cited: 331
727 38

728 R. C. Goldman, L. Leive, *Eur. J. Biochem.* 1980, 107, 145.
729 Wiley Online Library | PubMed | CAS | Web of Science® Times Cited: 353

730 39

731 T. Miyamoto, S. Okano, N. Kasai, *Appl. Environ. Microbiol.* 2009, 75, 5058.

732 CrossRef | PubMed | CAS | Web of Science® Times Cited: 9

733 40

734 H. Mrazova, J. Koller, G. Fajerikova, P. Babal, *Cell Tissue Bank* 2014, 15, 429.

735 CrossRef | PubMed | CAS | Web of Science® Times Cited: 2

736 41

737 P. S-Juan, H. J. T. Ward, R. De Silva, R. S. G. Knight, R. G. Will, *Br. J. Ophthalmol.* 2004,

738 88, 446.

739 CrossRef | PubMed | CAS | Web of Science® Times Cited: 6

740 42

741 S. Lerouge, *Sterilization of Biomaterials and Medical Devices* (Eds.: S. Lerouge, A.

742 Simmone), Woodhead Publishing Limited, Cambridge, UK 2012, p. 10.

743 CrossRef

744 43

745 M. M. Tuney, M. M. Tunney, N. Dunne, G. Einarsson, A. McDowell, A. Kerr, S. Patrick, J.

746 *Ortho. Res.* 2007, 25, 2.

747 Wiley Online Library | CAS | Web of Science® Times Cited: 37

748 44

749 P. Selves, V. Mirabet, M. Alvarez, *World J. Gastroenterol.* 2014, 20, 7434.

750 CrossRef | PubMed | Web of Science® Times Cited: 1

751 45

752 M. Silindir, A. Yekta Ozer, *FABAD J. Pharm. Sci.* 2009, 34, 43.

753 46

754 N. Yusof, *Radiation in Tissue Banking – Basic Science and Clinical Applications of*

755 *Irradiated Tissue Allografts* (Eds.: A. Nather, N. Yusof, N. Hilmy), © World Scientific

756 Publishing Co. Pte. Ltd., Singapore 2007, p. 129.

757 47

758 D. R. McAllister, M. J. Joyce, B. J. Mann, C. T. Vangsness, Jr., *Am. J. Sports Med.* 2007, 35,

759 2148.

760 CrossRef | PubMed | Web of Science® Times Cited: 69

761 48

762 F. von Versen-Hoyneck, C. Syring, S. Bachmann, D. E. Moller, *Cell Tissue Bank* 2004, 5, 45.

763 CrossRef | PubMed

764 49

765 ISO-17665, Sterilization of health care products — Moist heat — Part 1: Requirements for
 766 the development, validation and routine control of a sterilization process for medical devices
 767 in The International Organization for Standardization. 2006: Geneva, Switzerland.

768 50

769 V. C. Abraham, D. L. Taylor, J. R. Haskins, Trends Biotechnol. 2004, 22, 15.

770 CrossRef | PubMed | CAS | Web of Science® Times Cited: 185

771 51

772 ISO-11137-2, Sterilization of health care products – Radiation – Part 2: Establishing the
 773 sterilization dose., in International Organization for Standardization. 2013: Geneva,
 774 Switzerland.

775 52

776 Microbiological Surveillance Program and Process Validation American Association of
 777 Tissue Banks, McLean, Virginia 2012.

778 53

779 Q. Q. Qiu, W. Q. Sun, J. Connor, Comprehensive Biomaterials (Ed.: P. Ducheyne), Elsevier,
 780 Amsterdam, The Netherlands 2011, p. 127.

781 CrossRef

782 54

783 A. Dziedzic-Goclawska, A. Kaminski, I. Uhrynowska-Tyszkiewicz, W. Stachowicz, Cell
 784 Tissue Bank 2005, 6, 201.

785 CrossRef | PubMed | CAS

786 55

787 C. R. Balsly, A. T. Cotter, L. A. Williams, B. D. Gaskins, M. A. Moore, L. Wolfenbarger, Jr.,
 788 Cell Tissue Bank 2008, 9, 289.

789 CrossRef | PubMed | Web of Science® Times Cited: 49

790 56

791 R. Singh, P. Gupta, P. Kumar, A. Kumar, M. P. Chacharkar, Cell Tissue Bank 2003, 4, 95.

792 CrossRef | PubMed

793 57

794 N. Marsit, S. Dwejen, I. Saad, S. Abdalla, A. Shaab, S. Salem, E. Khanfas, A. Hasan, M.
 795 Mansur, M. Abdul Sammad, Cell Tissue Bank 2014, 15, 603.

796 CrossRef | PubMed | Web of Science® Times Cited: 1

797 58

798 Radiation sterilization of tissue allografts: requirements for validation and routine control: a
799 code of practice, International Atomic Energy Agency, Vienna 2007.
800 59
801 S. Endres, M. Kratz, J. Musculoskelet Neuronal Interact 2009, 9, 25.
802 PubMed | Web of Science® Times Cited: 5
803 60
804 B. E. Butterworth, J. R. Chapman, Regul. Toxicol. Pharmacol. 2007, 49, 149.
805 CrossRef | PubMed | CAS | Web of Science® Times Cited: 2
806 61
807 D. W. Jackson, G. E. Windler, T. M. Simon, Am. J. Sports Med. 1990, 18, 1.
808 CrossRef | PubMed | CAS | Web of Science® Times Cited: 194
809 62
810 A. White, D. Burns, T. W. Christensen, J. Biotechnol. 2006, 123, 504.
811 CrossRef | PubMed | CAS | Web of Science® Times Cited: 74
812 63
813 E. Shieh, A. Paszczynski, C. M. Wai, Q. Lang, R. L. Crawford, J. Microbiol. Methods 2009,
814 76, 247.
815 CrossRef | PubMed | CAS | Web of Science® Times Cited: 18
816 64
817 W. A. Rutala, D. J. Weber, Am. J. Infect. Control 2013, 41, S2.
818 CrossRef | PubMed | Web of Science® Times Cited: 18
819 65
820 A. Simmons, Sterilization of Biomaterials and Medical Devices. (Eds.: S. Lerouge, A.
821 Simmone), Woodhead Publishing Limited, Cambridge, UK 2012, p. 310.
822 CrossRef
823 66
824 M. Perrut, J. Supercrit Fluids 2012, 66, 359.
825 CrossRef | CAS | Web of Science® Times Cited: 21
826 67
827 M. S. a. H. P. P. Wutzler, J. Clin. Microbiol. 1975, 1, 246.
828 PubMed | Web of Science® Times Cited: 1
829 68
830 C. S. Frauke von Versen-Höyneck, S. Bachmann, D. E. Möller, Cell Tissue Bank 2004a, 5, 45.
831 CrossRef

832 69

833 P. D. Kemp, Peracetic Acid Sterilization of Collagen or Collagenous Tissue (Ed.: U. S.

834 Patent), Organogenesis Inc., Canton, Mass, USA 1995.

835 70

836 A. Pruss, C. Perka, P. Degenhardt, U. Maronna, K. Buttner-Janz, B. Paul, K. Muller, C.

837 Klumpp, J. C. Bruck, R. Von Versen, Cell Tissue Bank 2002, 3, 235.

838 CrossRef | PubMed | CAS

839 71

840 W. A. Rutala, D. J. Weber, Am. J. Infect. Control 2013, 41, S2.

841 CrossRef | PubMed | Web of Science® Times Cited: 18

842 72

843 S. Killeen, M. McCourt, Surgery 2012, 30, 687.

844 73

845 W. A. Rutala, D. J. Weber, J. Hosp. Infect. 1999, 43, S43.

846 CrossRef | PubMed | Web of Science® Times Cited: 55

847 74

848 K. Shimizu, H. Yano, E. Nakamura, N. Kaku, Ann. Transplant. 2001, 6, 26.

849 PubMed

850 75

851 M. N. Bathina, S. Mickelsen, C. Brooks, J. Jaramillo, T. Hepton, F. M. Kusumoto, J. Am.

852 Coll. Cardiol. 1998, 32, 1384.

853 CrossRef | PubMed | CAS | Web of Science® Times Cited: 20

854 76

855 S. D. Ferreira, W. S. Dernell, B. E. Powers, R. A. Schochet, C. A. Kuntz, S. J. Withrow, R. M.

856 Wilkins, Clin. Orthop. Relat. Res. 2001, 388, 233.

857 CrossRef

858 77

859 Y. Ikarashi, T. Tsuchiya, A. Nakamura, Biomaterials 1995, 16, 177.

860 CrossRef | PubMed | CAS | Web of Science® Times Cited: 20

861 78

862 G. Fridman, G. Friedman, A. Gutsol, A. B. Shekhter, V. N. Vasilets, A. Fridman, Plasma

863 Process Polym. 2008, 5, 503.

864 Wiley Online Library | CAS | Web of Science® Times Cited: 722

865 79

866 J. Heinlin, G. Morfill, M. Landthaler, W. Stolz, G. Isbary, J. L. Zimmermann, T. Shimizu, S.
 867 Karrer, J. Dtsch. Dermatol. Ges. 2010, 8, 968.
 868 PubMed | Web of Science® Times Cited: 85
 869 80
 870 M. Moreau, N. Orange, M. G. Feuilleley, Biotechnol. Adv. 2008, 26, 610.
 871 CrossRef | PubMed | CAS | Web of Science® Times Cited: 190
 872 81
 873 M. G. Kong, G. Kroesen, G. Morfill, T. Nosenko, T. Shimizu, J. van Dijk, J. L. Zimmermann,
 874 New J. Phys. 2009, 11, 115012.
 875 CrossRef | Web of Science® Times Cited: 587 | ADS
 876 82
 877 C. Cheng, L. Peng, X. Lei, Z. Li-Ye, Z. Ru-J., Chin. Phys. 2006, 15, 1544.
 878 CrossRef | CAS | Web of Science® Times Cited: 30 | ADS
 879 83
 880 O. Schlüter, J. Ehlbeck, C. Hertel, M. Habermeyer, A. Roth, K. H. Engel, T. Holzhauser, D.
 881 Knorr, G. Eisenbrand, Mol. Nutr. Food Res. 2013, 57, 920.
 882 Wiley Online Library | PubMed | CAS | Web of Science® Times Cited: 25
 883 84
 884 B. Haertel, T. von Woedtke, K.-D. Weltmann, U. Lindequist, Biomol. Ther. 2014, 22, 477.
 885 CrossRef | CAS | Web of Science® Times Cited: 32
 886 85
 887 R. Morent, N. De Geyter, Biomedical Engineering – Frontiers and Challenges (Ed.: R. Fazel),
 888 In Tech, Rijeka, Croatia 2011, p. 25.
 889 86
 890 L. Bárdos, H. Baránková, Vacuum 2008, 83, 522.
 891 CrossRef | CAS | Web of Science® Times Cited: 16 | ADS
 892 87
 893 K. P. Arjunan, V. K. Sharma, S. Ptasinska, Int. J. Mol. Sci. 2015, 16, 2971.
 894 CrossRef | PubMed | Web of Science® Times Cited: 11
 895 88
 896 M. Y. Alkawareek, S. P. Gorman, W. G. Graham, B. F. Gilmore, Int. J. Antimicrob. Agents
 897 2014, 43, 154.
 898 CrossRef | PubMed | CAS | Web of Science® Times Cited: 17
 899 89

900 S. A. Ermolaeva, A. F. Varfolomeev, M. Y. Chernukha, D. S. Yurov, M. M. Vasiliev, A. A.
 901 Kaminskaya, M. M. Moisenovich, J. M. Romanova, A. N. Murashev, I. I. Selezneva, T.
 902 Shimizu, E. V. Sysolyatina, I. A. Shaginyan, O. F. Petrov, E. I. Mayevsky, V. E. Fortov, G. E.
 903 Morfill, B. S. Naroditsky, A. L. Gintsburg, J. Med. Microbiol. 2011, 60, 75.
 904 CrossRef | PubMed | CAS | Web of Science® Times Cited: 86
 905 90
 906 G. Fridman, G. Friedman, A. Gutsol, A. B. Shekhter, V. N. Vasilets, A. Fridman, Plasma
 907 Process Polym. 2008, 5, 503.
 908 Wiley Online Library | CAS | Web of Science® Times Cited: 722
 909 91
 910 X. Han, W. A. Cantrell, E. E. Escobara, S. Ptasinskab, Eur. Phys. J. D 2014, 68, 46.
 911 CrossRef | CAS | Web of Science® Times Cited: 7 | ADS
 912 92
 913 C. Sadiqali, M. Černák, M. Pavel, H. Josef, J. Appl. Biomed. 2010, 8, 55.
 914 CrossRef | CAS | Web of Science® Times Cited: 39
 915 93
 916 S. Emmert, F. Brehmer, H. Hänßle, A. Helmke, N. Mertens, R. Ahmed, D. Simon, D.
 917 Wandke, W. Maus-Friedrichs, G. Däschlein, M. P. Schön, W. Viöl, Clin. Plasma Med. 2013,
 918 1, 24.
 919 CrossRef
 920 94
 921 G. Daeschlein, S. Scholz, R. Ahmed, T. von Woedtke, H. Haase, M. Niggemeier, E. Kindel,
 922 R. Brandenburg, K. D. Weltmann, M. Juenger, J. Hosp. Infect. 2012, 81, 177.
 923 CrossRef | PubMed | Web of Science® Times Cited: 38
 924 95
 925 A. S. Wu, S. Kalghatgi, D. Dobrynin, R. Sensenig, E. Cerchar, E. Podolsky, E. Dulaimi, M.
 926 Paff, K. Wasko, K. P. Arjunan, K. Garcia, G. Fridman, M. Balasubramanian, R. Ownbey, K.
 927 A. Barbee, A. Fridman, G. Friedman, S. G. Joshi, A. D. Brooks, J. Surg. Res. 2013, 179, e1.
 928 CrossRef | PubMed | Web of Science® Times Cited: 18
 929 96
 930 B. Yang, J. Chen, Q. Yu, H. Li, M. Lin, A. Mustapha, L. Hong, Y. Wang, J. Dent. 2011, 39,
 931 48.
 932 CrossRef | PubMed | Web of Science® Times Cited: 33
 933 97

934 X. Zhou, Z. Xiong, Y. Cao, X. Lu, D. Liu, *IEEE Trans. Plasma Sci.* 2010, 38, 3370.
 935 CrossRef | Web of Science® Times Cited: 14 | ADS
 936 98
 937 N. O'Connor, O. Cahill, S. Daniels, S. Galvin, H. Humphreys, *J. Hosp. Infect.* 2014, 88, 59.
 938 CrossRef | PubMed | Web of Science® Times Cited: 17
 939 99
 940 M. R. Boscariol, A. J. Moreira, R. D. Mansano, I. S. Kikuchi, T. J. Pinto, *Int. J. Pharm.* 2008,
 941 353, 170.
 942 PubMed | Web of Science® Times Cited: 11
 943 100
 944 E. Curran, R. Duffy, D. Peretz, S. Park, B. Seiber, R. Smalley, A. Raghavan, M. Gurjar, D.
 945 Dobrynin, K. Wasko, A. Fridman, G. Fridman, D. Paog, *Plasma Med.* 2013, 3, 153.
 946 CrossRef
 947 101
 948 G. Avramidis, B. Stüwe, R. Wascher, M. Bellmann, S. Wieneke, A. von Tiedemann, W. Viöl,
 949 *Surf. Coat. Technol.* 2010, 205, S405.
 950 CrossRef | CAS | Web of Science® Times Cited: 7
 951 102
 952 S. Ptasinska, B. Bahnev, A. Stypczynska, M. Bowden, N. J. Mason, N. S. Braithwaite, *Phys.*
 953 *Chem. Chem. Phys.* 2010, 12, 7779.
 954 CrossRef | PubMed | CAS | Web of Science® Times Cited: 27
 955 103
 956 E. Stoffels, Y. Sakiyama, D. B. Graves, *Plasma Sci. IEEE Trans.* 2008, 36, 1441.
 957 CrossRef | CAS | Web of Science® Times Cited: 182 | ADS
 958 104
 959 D. A. Mendis, M. Rosenberg, F. Azam, *IEEE Trans. Plasma Sci.* 2000, 28, 1304.
 960 CrossRef | Web of Science® Times Cited: 90 | ADS
 961 105
 962 J. L. Zimmermann, T. Shimizu, H. U. Schmidt, Y. F. Li, G. E. Morfill, G. Isbary, *New J.*
 963 *Phys.* 2012, 14, 073037.
 964 CrossRef | Web of Science® Times Cited: 17 | ADS
 965 106
 966 M. Laroussi, F. Leipold, *Int. J. Mass Spectrom.* 2004, 233, 81.
 967 CrossRef | CAS | Web of Science® Times Cited: 324 | ADS

968 107

969 M. Laroussi, *Plasma Process Polym.* 2005, 2, 391.

970 Wiley Online Library | CAS | Web of Science® Times Cited: 492

971 108

972 M. L. Burts, I. Alexeff, E. T. Meek, J. A. McCullers, *Am. J. Infect. Control* 2009, 37, 729.

973 CrossRef | PubMed | Web of Science® Times Cited: 21

974 109

975 E. Kvam, B. Davis, F. Mondello, A. L. Garner, *Antimicrob. Agents Chemother.* 2012, 56,

976 2028.

977 CrossRef | PubMed | CAS | Web of Science® Times Cited: 39

978 110

979 T. Maisch, T. Shimizu, Y. F. Li, J. Heinlin, S. Karrer, G. Morfill, J. L. Zimmermann, *PLoS*

980 *ONE* 2012, 7, e34610.

981 CrossRef | PubMed | Web of Science® Times Cited: 47 | ADS

982 111

983 T. Maisch, T. Shimizu, A. Mitra, J. Heinlin, S. Karrer, Y. F. Li, G. Morfill, J. L.

984 Zimmermann, *J. Ind. Microbiol. Biotechnol.* 2012, 39, 1367.

985 CrossRef | PubMed | CAS | Web of Science® Times Cited: 13

986 112

987 C. M. Edelblute, M. A. Malik, L. C. Heller, *Bioelectrochemistry* 2015, 103, 22.

988 CrossRef | PubMed | CAS | Web of Science® Times Cited: 4

989 113

990 M. Korachi, C. Gurol, N. Aslan, *J. Electrostat.* 2010, 68, 508.

991 CrossRef | CAS | Web of Science® Times Cited: 20

992 114

993 A. Fernandez, N. Shearer, D. R. Wilson, A. Thompson, *Int. J. Food. Microbiol.* 2012, 152,

994 175.

995 CrossRef | PubMed | Web of Science® Times Cited: 25

996 115

997 J. J. Cotter, P. Maguire, F. Soberon, S. Daniels, J. P. O'Gara, E. Casey, *J. Hosp. Infect.* 2011,

998 78, 204.

999 CrossRef | PubMed | Web of Science® Times Cited: 19

1000 116

1001 C. Wei, H. Jun, D. Ning, L. Xiao-Di, L. Guo-Hua, W. Xing-Quan, Z. Guo-Ping, G. Li-Hong,
 1002 Y. Si-Ze, Chin. Phys. Lett. 2012, 29, 075203.
 1003 CrossRef | CAS | Web of Science® Times Cited: 3 | ADS
 1004 117
 1005 R. Matthes, C. Bender, R. Schluter, I. Koban, R. Bussiahn, S. Reuter, J. Lademann, K. D.
 1006 Weltmann, A. Kramer, PLoS ONE 2013, 8, e70462.
 1007 CrossRef | PubMed | Web of Science® Times Cited: 15 | ADS
 1008 118
 1009 O. Lademann, A. Kramer, H. Richter, A. Patzelt, M. Meinke, J. Roewert-Huber, V. Czaika, K.
 1010 Weltmann, B. Hartmann, S. Koch, Laser Phys. Lett. 2011, 8, 313.
 1011 Wiley Online Library | Web of Science® Times Cited: 19
 1012 119
 1013 O. Lademann, A. Kramer, H. Richter, A. Patzelt, M. Meinke, V. Czaika, K. -D. Weltmann, B.
 1014 Hartmann, S. Koch, Skin Pharmacol. Physiol. 2011, 24, 284.
 1015 CrossRef | PubMed | CAS | Web of Science® Times Cited: 26
 1016 120
 1017 A. Ali, Y. H. Kim, J. Y. Lee, S. Lee, H. S. Uhm, G. Cho, B. J. Park, E. H. Choi, Curr. Appl.
 1018 Phys. 2014, 14, S142.
 1019 CrossRef | Web of Science® Times Cited: 1
 1020 121
 1021 Y. F. Hong, J. G. Kang, H. Y. Lee, H. S. Uhm, E. Moon, Y. H. Park, Lett. Appl. Microbiol.
 1022 2009, 48, 33.
 1023 Wiley Online Library | PubMed | CAS | Web of Science® Times Cited: 44
 1024 122
 1025 S. Shimizu, S. Barczyk, P. Rettberg, T. Shimizu, T. Klaempfl, J. L. Zimmermann, T.
 1026 Hoeschen, C. Linsmeier, P. Weber, G. E. Morfill, H. M. Thomas, Plant. Space Sci. 2014, 90,
 1027 60.
 1028 CrossRef | Web of Science® Times Cited: 7 | ADS
 1029 123
 1030 J. Jeon, T. Klaempfl, J. Zimmermann, G. Morfill, T. Shimizu, New J. Phys. 2014, 16, 103007.
 1031 CrossRef | Web of Science® Times Cited: 2 | ADS
 1032 124
 1033 S. Patil, T. Moiseev, N. N. Misra, P. J. Cullen, J. P. Mosnier, K. M. Keener, P. Bourke, J.
 1034 Hosp. Infect. 2014, 88, 162.

1035 CrossRef | PubMed | Web of Science® Times Cited: 10
 1036 125
 1037 F. Rossi, O. Kylián, Sterilisation of Biomaterials and Medical Devices (Eds.: S. Lerouge, A.
 1038 Simmons), Woodhead Publishing Series in Biomaterials, Philadelphia, USA 2012, p. 117.
 1039 CrossRef
 1040 126
 1041 H. Shintani, Biocontrol. Sci. 2016, 21, 63.
 1042 CrossRef | PubMed | Web of Science®
 1043 127
 1044 B. J. Park, K. Takatori, M. H. Lee, D. -W. Han, Y. I. Woo, H. J. Son, J. K. Kim, K.-H. Chung,
 1045 S. O. Hyun, J.-C. Park, Surf. Coat. Technol. 2007, 201, 5738.
 1046 CrossRef | CAS | Web of Science® Times Cited: 29
 1047 128
 1048 D. L. Bayliss, J. L. Walsh, G. Shama, F. Iza, M. G. Kong, New J. Phys. 2009, 11, 115024.
 1049 CrossRef | Web of Science® Times Cited: 26 | ADS
 1050 129
 1051 J. Julák, O. Janoušková, V. Scholtz, K. Holada, Plasma Process Polym. 2011, 8, 316.
 1052 Wiley Online Library | CAS | Web of Science® Times Cited: 17
 1053 130
 1054 A. Holmberg, R. Lood, M Mörgelin, B. Söderquist, E. Holst, M. Collin, B. Christensson, M.
 1055 Rasmussen, Clin. Microbiol. Infect. 2009, 15, 787.
 1056 Wiley Online Library | PubMed | Web of Science® Times Cited: 53
 1057 131
 1058 T. Maisch, T. Shimizu, G. Isbary, J. Heinlin, S. Karrer, T. G. Klampfl, Y. F. Li, G. Morfill, J.
 1059 L. Zimmermann, Appl. Environ. Microbiol. 2012, 78, 4242.
 1060 CrossRef | PubMed | CAS | Web of Science® Times Cited: 31
 1061 132
 1062 K. Fricke, I. Koban, H. Tresp, L. Jablonowski, K. Schroder, A. Kramer, K. D. Weltmann, T.
 1063 von Woedtke, T. Kocher, PLoS ONE 2012, 7, e42539.
 1064 CrossRef | PubMed | Web of Science® Times Cited: 35 | ADS
 1065 133
 1066 H. Yasuda, T. Miura, H. Kurita, K. Takashima, A. Mizuno, Plasma Process Polym. 2010, 7,
 1067 301.
 1068 Wiley Online Library | CAS | Web of Science® Times Cited: 45

1069 134

1070 A. Mai-Prochnow, A. B. Murphy, K. M. McLean, M. G. Kong, K. K. Ostrikov, *Int. J.*
 1071 *Antimicrob. Agents* 2014, 43, 508.

1072 CrossRef | PubMed | CAS | Web of Science® Times Cited: 35

1073 135

1074 S. Bekeschus, A. Schmidt, K.-D. Weltmann, T. von Woedtke, *Clin. Plasma Med.* 2016, 4, 19.

1075 CrossRef

1076 136

1077 F. Brehmer, H. A. Haenssle, G. Daeschlein, R. Ahmed, S. Pfeiffer, A. Gorlitz, D. Simon, M.
 1078 P. Schon, D. Wandke, S. Emmert, *J. Eur. Acad. Dermatol. Venereol.* 2015, 29, 148.

1079 Wiley Online Library | PubMed | CAS | Web of Science® Times Cited: 20

1080 137

1081 E. Stoffels, I. E. Kieft, R. E. J. Sladek, *J. Phys. D Appl. Phys.* 2003, 36, 2908.

1082 CrossRef | CAS | Web of Science® Times Cited: 136 | ADS

1083 138

1084 T Jiang, H. Zhao, C. Wang, G. Rao, A. Li, H. Tolner, B. Li, *Plasma Med.* 2012, 2, 179.

1085 CrossRef

1086 139

1087 E. Stoffels, A. J. Flikweert, W. W. Stoffels, G. M. W. Kroesen, *Plasma Sources Sci. Technol.*
 1088 2002, 11, 383.

1089 CrossRef | CAS | Web of Science® Times Cited: 355 | ADS

1090 140

1091 C. Welz, S. Becker, Y.-F. Li, T. Shimizu, J. Jeon, S. Schwenk-Zieger, H. M. Thomas, G.
 1092 Isbary, G. E. Morfill, U. Harréus, *J. Phys. D Appl. Phys.* 2013, 46, 045401.

1093 CrossRef | CAS | Web of Science® Times Cited: 10 | ADS

1094 141

1095 X. Pei, X. Lu, J. Liu, D. Liu, Y. Yang, K. Ostrikov, K. C. Paul, Y. Pan, *J. Phys. D Appl. Phys.*
 1096 2012, 45, 165205.

1097 CrossRef | CAS | Web of Science® Times Cited: 44 | ADS

1098 142

1099 D. Dobrynin, G. Fridman, G. Friedman, A. Fridman, *New J. Phys.* 2009, 11, 115020.

1100 CrossRef | ADS

1101 143

1102 A. H. Tehrani, P. Davari, S. Singh, A. Oloyede, *J. Mater. Sci. Mater. Med.* 2014, 25, 953.

1103 CrossRef | PubMed | CAS | Web of Science® Times Cited: 3
 1104 144
 1105 E. J. Szili, J. W. Bradley, R. D. Short, J. Phys. D 2014, 47, 152002.
 1106 CrossRef | CAS | Web of Science® Times Cited: 22 | ADS
 1107 145
 1108 D. Dobrynin, G. Fridman, G. Friedman, A. A. Fridman, Plasma Med. 2012, 2, 71.
 1109 CrossRef
 1110 146
 1111 C. X. Wang, Y. Liu, H. L. Xu, Y. Ren, Y. P. Qiu, Appl. Surf. Sci. 2008, 254, 2499.
 1112 CrossRef | CAS | Web of Science® Times Cited: 51 | ADS
 1113 147
 1114 C. X. Wang, Y. P. Qiu, Surf. Coat. Technol. 2007, 201, 6273.
 1115 CrossRef | CAS | Web of Science® Times Cited: 69
 1116 148
 1117 K. Heuer, M. A. Hoffmanns, E. Demir, S. Baldus, C. M. Volkmar, M. Rohle, P. C. Fuchs, P.
 1118 Awakowicz, C. V. Suschek, C. Oplander, Nitric Oxide 2015, 44, 52.
 1119 CrossRef | PubMed | CAS | Web of Science® Times Cited: 13
 1120 149
 1121 F. von Versen-Hoeyneck, A. P. Steinfeld, J. Becker, M. Hermel, W. Rath, U. Hesselbarth,
 1122 Biologicals 2008, 36, 248.
 1123 CrossRef | PubMed | CAS | Web of Science® Times Cited: 17
 1124 150
 1125 E. Noriega, G. Shama, A. Laca, M. Díaz, M. G. Kong, Food Microbiol. 2011, 28, 1293.
 1126 CrossRef | PubMed | CAS | Web of Science® Times Cited: 59
 1127 151
 1128 S. S. Ab Hamid, N. K. Zahari, N. Yusof, A. Hassan, Cell Tissue Bank 2014, 15, 15.
 1129 CrossRef | PubMed | Web of Science® Times Cited: 5
 1130 152
 1131 Z. Nor Kamilia, Y. N. Suzina SAH, Regen. Res. 2014, 3, 64.
 1132 153
 1133 R. Singh, M. P. Chacharkar, J. Tissue Viability 2011, 20, 49.
 1134 CrossRef | PubMed | Web of Science® Times Cited: 7
 1135 154
 1136 S. Kitazaki, A. Tanaka, N. Hayashi, Vacuum 2014, 110, 217.

1137 CrossRef | CAS | Web of Science® Times Cited: 5 | ADS
 1138 155
 1139 M. Annunziata, L. Canullo, G. Donnarumma, P. Caputo, L. Nastri, L. Guida, Med. Oral Patol.
 1140 Oral Cir. Bucal 2016, 21, e118.
 1141 CrossRef | PubMed | Web of Science® Times Cited: 1
 1142 156
 1143 E. Simoncelli, D. Barbieri, R. Laurita, A. Liguori, A. Stancampiano, L. Viola, R. Tonini, M.
 1144 Gherardi, V. Colombo, Clin. Plasma Med. 2015, 3, 77.
 1145 CrossRef
 1146 157
 1147 C.-W. Kan, C.-F. Lam, C.-K. Chan, S.-P. Ng, Carbohydr. Polym. 2014, 102, 167.
 1148 CrossRef | PubMed | CAS | Web of Science® Times Cited: 10
 1149 158
 1150 L. Bárdos, H. Baránková, Thin Solid Films 2010, 518, 6705.
 1151 CrossRef | CAS | Web of Science® Times Cited: 85 | ADS
 1152 159
 1153 C. Wang, Y. Qiu, Surf. Coat. Technol. 2007, 201, 6273.
 1154 CrossRef | CAS | Web of Science® Times Cited: 69
 1155 160
 1156 S. Lerouge, M. R. Wertheimer, L. Yahia, Plasmas Polym. 2001, 6, 175.
 1157 CrossRef | CAS
 1158 161
 1159 E. Stoffels, I. E. Kieft, R. E. J. Sladek, L. J. M. v. d. Bedem, E. P. v. d. Laan, M. Steinbu,
 1160 Plasma Sources Sci. Technol. 2006, 15, S169.
 1161 CrossRef | CAS | Web of Science® Times Cited: 173 | ADS
 1162 162
 1163 N. De Geyter, R. Morent, Annu. Rev. Biomed. Eng. 2012, 14, 255.
 1164 CrossRef | PubMed | CAS | Web of Science® Times Cited: 26
 1165 163
 1166 S. Pankaj, N. Misra, P. Cullen, Innov. Food Sci. Emerg. Technol. 2013, 19, 153.
 1167 CrossRef | CAS | Web of Science® Times Cited: 29
 1168 164
 1169 H. Eto, Y. Ono, A. Ogino, M. Nagatsu, Appl. Phys. Lett. 2008, 93, 221502.
 1170 CrossRef | CAS | Web of Science® Times Cited: 36 | ADS

1171 165

1172 T. Lee, P. Puligundla, C. Mok, Food Control 2015, 51, 149.

1173 CrossRef | PubMed | CAS | Web of Science® Times Cited: 7

1174 166

1175 H. I. Yong, H. -J. Kim, S. Park, A. U. Alahakoon, K. Kim, W. Choe, C. Jo, Food Microbiol.

1176 2015, 46, 46.

1177 CrossRef | PubMed | CAS | Web of Science® Times Cited: 14

1178 167

1179 O. V. Penkov, M. Khadem, W. -S. Lim, D. -E. Kim, J. Coat. Technol. Res. 2015, 12, 225.

1180 CrossRef | CAS | Web of Science® Times Cited: 8

1181 168

1182 C. Wiegand, M. Abel, P. Ruth, T. Wilhelms, D. Schulze, J. Norgauer, U. -C. Hipler, J.

1183 Biomed. Mater. Res. B Appl. Biomater. 2009, 90, 710.

1184 Wiley Online Library | PubMed | CAS | Web of Science® Times Cited: 21

1185 169

1186 E. Y. Elenes, S. A. Hunter, J. Bone Joint Surg. Am. 2014, 96, 1321.

1187 CrossRef | PubMed | Web of Science® Times Cited: 3

1188 170

1189 C. M. Deeley, Radiat. Phys. Chem. 2004, 71, 505.

1190 CrossRef | CAS | Web of Science® Times Cited: 1 | ADS

1191 171

1192 D. Cheung, N. Perelman, D. Tong, M. Nimni, J. Biomed. Mater. Res. 1990, 24, 581.

1193 Wiley Online Library | PubMed | CAS | Web of Science® Times Cited: 95

1194 172

1195 S. Baloda, J. Martin, J. Carter, E. Jenness, B. Judd, K. Smeltz, I. Uettwiller, M. Hockstad,

1196 Guide to irradiation and sterilization of single-use bioprocess components and systems. The

1197 Society of the Plastics Industry, Inc. The irradiation and sterilization subcommittee of the

1198 bioprocess systems alliance, 2008, 2, 10.

1199 173

1200 A. Hoburg, S. Keshlaf, T. Schmidt, M. Smith, U. Gohs, C. Perka, A. Pruss, S. Scheffler, Cell

1201 Tissue Bank 2014, 16, 219.

1202 CrossRef | PubMed | CAS | Web of Science® Times Cited: 2

1203 174

1204 M. Smith, R. Galloway, Radiat. Phys. Chem. 2004, 71, 531.

1205 CrossRef | CAS | Web of Science® | ADS
 1206 175
 1207 G. da Cunha Mendez, T. da Silva Brandao, C. Miranda Silva, Expert Rev. Med. Devices
 1208 2008, 5, 323.
 1209 CrossRef | PubMed | CAS
 1210 176
 1211 G. C. Mendes, T. R. Brandao, C. L. Silva, Am. J. Infect. Control 2007, 35, 574.
 1212 CrossRef | PubMed | Web of Science® Times Cited: 66
 1213 177
 1214 T. M. Moore, E. Gendler, J. Orthop. Res. 2004, 22, 1358.
 1215 Wiley Online Library | PubMed | CAS | Web of Science® Times Cited: 10
 1216 178
 1217 A. Nather, J. L. L. Chew, Z. Aziz, Radiation in Tissue Banking – Basic Science and Clinical
 1218 Applications of Irradiated Tissue Allografts (Eds.: A. Nather, N. Yusof, N. Hilmy), © World
 1219 Scientific Publishing Co. Pte. Ltd., Singapore 2007.
 1220 CrossRef
 1221 179
 1222 ISO-10993-7, Biological evaluation of medical devices – Part 7: Ethylene oxide sterilization
 1223 residuals., in The International Organization for Standardization. 2008: Geneva, Swetzerland.
 1224 180
 1225 T. S. Roberts, D. Drez, Jr., W. McCarthy, R. Paine, Am. J. Sports Med. 1991, 19, 35.
 1226 CrossRef | PubMed | CAS | Web of Science® Times Cited: 109
 1227 181
 1228 Ethylene Oxide (EtO): Evidence of Carcinogenicity, U.S. Department of Health and Human
 1229 Services, National Institute for Occupational Safety and Health, USA 1981.
 1230 182
 1231 K. Steenland, E. Whelan, J. Deddens, L. Stayner, E. Ward, Cancer Causes Control 2003, 14,
 1232 531.
 1233 CrossRef | PubMed | Web of Science® Times Cited: 23
 1234 183
 1235 V. M. Steelman, AORN J. 1992, 55, 773.
 1236 CrossRef | PubMed | CAS
 1237 184

1238 Preventing worker injuries and deaths from explosions in industrial ethylene oxide
 1239 sterilization facilities, Public Health Service, Centers for Disease Control and Prevention,
 1240 National Institute for Occupational Safety and Health, Atlanta, GA 2007.
 1241 185
 1242 C. T. Vangsness, Jr., P. P. Wagner, T. M. Moore, M. R. Roberts, *Arthroscopy* 2006, 22, 1351.
 1243 CrossRef | PubMed | Web of Science® Times Cited: 32
 1244 186
 1245 Y. C. Chien, H. H. Liu, Y. C. Lin, P. C. Su, L. H. Li, C. P. Chang, D. T. Tang, C. Y. Chen, J.
 1246 *Biomed. Mater. Res. B Appl. Biomater.* 2007, 83, 527.
 1247 Wiley Online Library | PubMed | CAS | Web of Science® Times Cited: 8
 1248 187
 1249 B. J. Park, K. Takatori, M. H. Lee, D.-W. Han, Y. I. Woo, H. J. Son, J. K. Kim, K.-H. Chung,
 1250 S. O. Hyun, J. -C. Park, *Surf. Coat. Technol.* 2007, 201, 5738.
 1251 CrossRef | CAS | Web of Science® Times Cited: 29
 1252 188
 1253 B. A. Niemira, *J. Food Sci.* 2012, 77, M171.
 1254 Wiley Online Library | PubMed | CAS | Web of Science® Times Cited: 29
 1255 189
 1256 A. Blumhagen, P. Singh, A. Mustapha, M. Chen, Y. Wang, Q. Yu, *Am. J. Dent.* 2014, 27, 84.
 1257 PubMed | Web of Science® Times Cited: 3
 1258 190
 1259 P. Sun, Y Sun, H. Wu, W. Zhu, J. L. Lopez, W. Liu, J. Zhang, R. Li, J. Fang, *Appl. Phys.*
 1260 *Lett.* 2011, 98, 021501.
 1261 CrossRef | CAS | Web of Science® Times Cited: 29 | ADS
 1262 191
 1263 B. Dasan, M. Mutlu, I. Boyaci, *Int. J. Food Microbiol.* 2016, 216, 50.
 1264 CrossRef | PubMed | CAS | Web of Science® Times Cited: 3
 1265 192
 1266 M. Selcuk, L. Oksuz, P. Basaran, *Bioresour. Technol.* 2008, 99, 5104.
 1267 CrossRef | PubMed | CAS | Web of Science® Times Cited: 80
 1268 193
 1269 N. S. Panikov, S. Paduraru, R. Crowe, P. J. Ricatto, C. Christodoulatos, K. Becker, *IEEE*
 1270 *Trans. Plasma Sci.* 2002, 30, 1424.
 1271 CrossRef | Web of Science® Times Cited: 43 | ADS

1272 194

1273 R. A. Venezia, M. Orrico, E. Houston, S. M. Yin, Y. Y. Naumova, *Infect. Control Hosp.*

1274 *Epidemiol.* 2008, 29, 430.

1275 CrossRef | PubMed | Web of Science® Times Cited: 35

1276 195

1277 N. Alshraideh, M. Alkawareek, S. Gorman, W. Graham, B. Gilmore, *J. Appl. Microbiol.*

1278 2013, 115, 1420.

1279 Wiley Online Library | PubMed | CAS | Web of Science® Times Cited: 12

1280 196

1281 O. Terrier, B. Essere, M. Yver, M. Barthélémy, M. Bouscambert-Duchamp, P. Kurtz, D.

1282 VanMechelen, F. Morfin, G. Billaud, O. Ferraris, *J. Clin. Virol.* 2009, 45, 119.

1283 CrossRef | PubMed | CAS | Web of Science® Times Cited: 22

1284 197

1285 D. Ziuzina, L. Han, P. J. Cullen, P. Bourke, *Int. J. Food Microbiol.* 2015, 210, 53.

1286 CrossRef | PubMed | Web of Science® Times Cited: 5

1287 198

1288 M. Moisan, P. Levif, J. Séguin, J. Barbeau, *J. Phys. D Appl. Phys.* 2014, 47, 285404.

1289 CrossRef | CAS | Web of Science® Times Cited: 1 | ADS

1290 199

1291 Q. Y. Nie, Z. Cao, C. S. Ren, D. Z. Wang, M. G. Kong, *New J. Phys.* 2009, 11, 115015.

1292 CrossRef | Web of Science® Times Cited: 44 | ADS

1293 200

1294 A. N. Aleynik, A. N. Baykov, M. B. Baskakov, G. T. Dambaev, O. I. Deneko, E. P.

1295 Krasnozhenov, E. V. Semichev, O. S. Zhdanova, *Strategic Technology (IFOST)*, 2012 7th

1296 International Forum, Tomsk Polytechnic University, Russia 2012.

1297 Related content

1298