


## Article

# Technological Advances in Ozone and Ozonized Water Spray Disinfection Devices

Luis Alberto Breda Mascarenhas <sup>1</sup>, Fabricia Oliveira Oliveira <sup>1</sup> , Eduardo Santos da Silva <sup>1</sup>, Laerte Marlon Conceição dos Santos <sup>1</sup>, Leticia de Alencar Pereira Rodrigues <sup>1</sup>, Paulo Roberto Freitas Neves <sup>1</sup>, Alex Álisson Bandeira Santos <sup>1</sup>, Greta Almeida Fernandes Moreira <sup>1</sup>, Gabriela Monteiro Lobato <sup>2</sup>, Carlos Nascimento <sup>2</sup>, Marcelo Gerhardt <sup>2</sup> and Bruna Aparecida Souza Machado <sup>1,\*</sup>

- <sup>1</sup> SENAI Institute of Innovation (ISI) in Health Advanced Systems (CIMATEC ISI SAS), University Center SENAI/CIMATEC, Salvador 41650-010, Brazil; breda@fiebr.org.br (L.A.B.M.); fabricia.oliveira@fbter.org.br (F.O.O.); eduardo.ss@fbter.org.br (E.S.d.S.); laerte.santos@fbter.org.br (L.M.C.d.S.); leticiap@fiebr.org.br (L.d.A.P.R.); PAULON@fiebr.org.br (P.R.F.N.); alex.santos@fiebr.org.br (A.Á.B.S.); greta.moreira@fiebr.org.br (G.A.F.M.)
- <sup>2</sup> CTG Brazil Group Rio Paraná Energia S.A. Rodovia MS-444 s/nº km 58, Ilha Solteira, Selviria 79590-000, Brazil; gabriela.lobato-ext@ctgbr.com.br (G.M.L.); carlos.nascimento@ctgbr.com.br (C.N.); marcelo.gerhardt@ctgbr.com.br (M.G.)
- \* Correspondence: brunam@fiebr.org.br; Tel.: +55-71-3879-5624



**Citation:** Mascarenhas, L.A.B.; Oliveira, F.O.; da Silva, E.S.; dos Santos, L.M.C.; de Alencar Pereira Rodrigues, L.; Neves, P.R.F.; Santos, A.Á.B.; Moreira, G.A.F.; Lobato, G.M.; Nascimento, C.; et al. Technological Advances in Ozone and Ozonized Water Spray Disinfection Devices. *Appl. Sci.* **2021**, *11*, 3081. <https://doi.org/10.3390/app11073081>

Academic Editor: Antonio Valero

Received: 10 March 2021

Accepted: 27 March 2021

Published: 30 March 2021

**Publisher's Note:** MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



**Copyright:** © 2021 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

**Abstract:** To control infectious diseases such as the severe acute respiratory syndrome coronavirus (Covid-19) that caused the current pandemic, disinfection measures are essential. Among building measures, disinfection chambers can help to decrease the transmission rate through the sanitizing capacity of the disinfectant used, which can thereby clean surfaces or humans. Out of existing biocides, ozone is considered one of the safest for humans, but one of the most powerful oxidizers, making the substance a better alternative as the biocidal solution in disinfection chambers. Analyses were carried out by using all patented documents related to disinfection chambers that used ozone as a disinfectant. A Derwent Innovation Index (DII) database search was undertaken to find these patents. Patent prospecting resulted in 620 patent documents that were divided into 134 patent families. There was no technology related to protective barriers for individuals, and the majority of patents in the retrieved data aimed at sterilizing medical devices and surfaces. Given that the specific Cooperative Patent Classification (CPC) code for ozone dissolved in liquid was used in the methodology search, but not included among the 10 most used codes in the patents, the use of ozonized water may be an innovative approach in the technology landscape of sterilization chambers.

**Keywords:** aqueous ozone; ozonated water; disinfection chambers; technological prospecting; patents

## 1. Introduction

Microbial infections caused by human pathogens follow a historical evolution in which they appear for the first time causing epidemics, undergo adaptations to become unstable pathogens, periodically reappear, and, in some cases, become endemic with the potential for future outbreaks [1]. The appearance of new human pathogens is usually related to the remodeling of relations between humans and microorganisms. Examples are human activity in geographical areas, the globalization of economic activities and culture, the spread of urbanization that allows for faster and more accessible contact, and hyperhygienic life that reduces exposure and creates tolerance to microorganisms [2]. Another example of this relationship is the current global pandemic related to the new coronavirus (SARS-CoV-2), a virus that displays high mortality rates, and of which the case fatality rate (CFR) has varied among countries [3]. SARS-CoV-2 (the causative agent of 2019 coronavirus disease (COVID-19)) is the result of viral recombinations that allowed for it to infect humans from breaking the animal–animal biological barrier to which it was related, thus characterizing itself as a zoonosis that, due to evidenced genetic relations, indicates

bats as the primary host [4]. Although most initial cases were associated with the place where the first patients visited—the seafood market in which the patients may have been infected by zoonotic or environmental exposure—it is the transmission between humans that enhances the epidemic characteristic of this infection [5]. This characteristic was and is being proven by studies indicating that the occurring pandemic is gradually growing due to the rapid transmission of SARS-CoV-2 among populations [4], generating great uncertainties for daily life and aggressively affecting the economy in several areas, mainly the aeronautical industry [6]. In addition, studies indicate that coronaviruses identified so far may only be the beginning of a series of revelations for newer and more serious zoonotic events [7].

Due to the current situation, concern about controlling the spread of respiratory viruses is growing [8]. In fact, contamination through contaminated surfaces and direct person-to-person contact is characterized as potential sources of dissemination of many pathogens, not only viral, but also bacterial and fungal [9,10]. Given these facts, it is extremely important to promote improvements in cleaning, disinfection, and sterilization processes of environmental surfaces and individuals in order to allow for safe interactions between humans and microbial pandemics that could arise [11]. Despite the effort and access to technologies that act for the control of infections, and contrary to expectations, their risks grow every day, affecting people's lives. This situation is aggravated by the increasing number of susceptible people to infections [12]. Therefore, the use of disinfectant solutions in environmental decontamination may be required in the fight against infections that, in addition to combating several emergent microorganisms, can help in the control of multiresistant microorganisms [13].

Surface disinfection was included in several national and international policies and recommendations to combat environmental infections. In contrast to hand hygiene, which is normally a daily activity, the opinion that environmental disinfection is important, and the methodologies and technologies that can support this process recently started to gain ground [14]. The introduction of protocols for carrying out surface-disinfection processes against this virus is, therefore, essential, especially in healthcare environments [15] since exposure to the virus is more pronounced in these places. Previous studies demonstrated the benefits of using ultraviolet-light devices for disinfecting hospital environments [16], portable devices with spraying systems for the decontamination of surfaces [17], and disinfection chambers with different biocidal agents [18,19], which drew attention with the SARS-CoV-2 pandemic. The development, advertising, and marketing of tunnels or cabins, or disinfection chambers have spread in several countries, although there is still no scientific evidence to support them [20]. City halls have installed this kind of system in several places, such as streets areas with heavy pedestrian traffic, highways, industries, malls, and offices [20]. It is usually set up at the entrances of, or inside, public transports [21,22]. These devices make use of substances such as sodium hypochlorite, ozonized water, ozone, or other biocidal agents [23].

In Brazil, this equipment was developed to meet the demand of institutions interested in disinfecting employees at workplace entrances and exits. Regarding the regulation of this equipment, the National Health Surveillance Agency (Anvisa) and other regulatory agencies clarified that there is no evidence that this measure is effective against the coronavirus pandemic [21,23]. The choice of chemical agent to be applied to these technologies is of paramount importance, and should be based on the recommendations of their manufacturers and on reports of agencies that alert and control the use of these substances in order to avoid safety and toxicity problems [24].

Among the list of sanitizers, one of the most promising biocide agents is ozone gas ( $O_{3(g)}$ ). It consists of a natural configuration of three oxygen atoms, and it has a half-life of about 1 h at room temperature, with subsequent degradation and the spontaneous formation of oxygen gas [25]. It is naturally produced by sunlight, involving nitrogen oxides and volatile organic compounds [26], and can also be produced from electricity generators [27].  $O_3$  has unique biological properties, acting as a powerful oxidizer against

viruses, bacteria, and protozoa; at recommended levels, it can be used as a microbicide gas and be dispersed in water [28].  $O_3$  leads to microbiological destruction through metabolic interferences. However, viral susceptibility might fluctuate in its presence. For example, for enveloped viruses, such as coronaviruses,  $O_3$  effectiveness may be more accentuated than that on nonenveloped viruses due to the  $O_3$  interaction with the envelopes of the lipid layer [28]. There are few studies that report the action of  $O_3$  on SARS-CoV-2 [29]. However, some authors reported  $O_3$  disinfection in the influenza A virus, respiratory syncytial virus [30], and SARS-CoV-1 [31], which can serve as reasonable substitutes in studies of  $O_3$  disinfection against SARS-CoV-2.  $O_3$  action is also proving effective against other types of microorganisms, expanding the possibilities of using this gas as a microbicide agent.

Nonetheless,  $O_3$  can be toxic in gaseous form; when dissolved in water, its degree of toxicity is reduced, and the sanitizing effect is maintained [32–35]. In addition,  $O_3$  dissolved in water (or ozonized water ( $O_{3(aq)}$ )) already has wide application in the treatment of dental diseases [36], and its use has been growing in other areas. Therefore, this substance can be a better alternative as a biocide solution in disinfection chambers. In fact,  $O_{3(aq)}$  has several advantages, being effective in reducing several pathogenic microorganisms, including not only viruses, but also bacteria and fungi [34,35,37]. In this sense, the use of  $O_{3(aq)}$ , associated with disinfection-chamber technology enables a range of uses both in the current pandemic and in other contexts where infectious diseases may spread.

Several disinfection chambers are being produced and commercialized with the purpose of being used by humans as a protective barrier. However, there are no scientific data that show evidence in this regard, given that those studies were limited to *in vitro* experiments. Limitations are likely related to challenges in human clinical research of which obstacles include obtaining committee approval, establishing clinical trials, recruiting participants, obtaining consent agreements, systematic reviews, and meta-analysis studies [38,39]. For this reason, it is extremely important to evaluate the effectiveness of these structures, so that their use by people is safely conducted, improving the current and emergency demand of COVID-19, and during future public-health demands in relation to protection against other infections.

Thus, in order to investigate the current development of technologies based on disinfection chambers using  $O_{3(g)}$  or  $O_{3(aq)}$ , this study examines the possibility of applying these devices, and identifies if there have been any applications for use as a protective barrier for individuals.

## 2. Materials and Methods

The study was based on technological prospection in order to collect technical and qualified information about disinfection chambers using  $O_{3(g)}$  or  $O_{3(aq)}$ . Data were obtained using the Derwent Innovation Index (DWPI) database, Thomson Innovation®, with license to use from SENAI CIMATEC University Center on 2 December 2020.

Data were obtained from the use of Cooperative Patent Classification (CPC) codes according to the following search strategy: (A61L2202/122) AND (A61L2/183 OR A61L2/202). Table 1 shows the meaning of each code used in technological prospecting, chosen from the formulation of a scope table (data not shown); analysis of the results was performed from the produced combinations.

**Table 1.** Cooperative Patent Classification (CPC) codes used in technological prospecting.

CPC Code	Related To
A61L 2202/122	Chambers for sterilization
A61L2/183	Ozone dissolved in a liquid
A61L2/202	Ozone (gas)

Since patent applications can be written in several languages, classification was used on the basis of CPC codes in order to obtain a broader research outcome, thereby resulting in the analysis of the largest number of patents in this area. As a result of technological

research, a total of 620 individual patents and 134 DWPI families were generated. Some patents may not appear in the search results because of the secrecy period of 18 months. GraphPad Prism 8.4 software (San Diego, CA, USA) was used for the construction of the graphs considering indicators of time analysis (priority year and expiry year), applicants (main applicants), status of patents, and main CPCs. Results concerning geographical distribution (main countries or regions, initial protection request locations, main competitor markets) and main technological areas were directly obtained from the DWPI database.

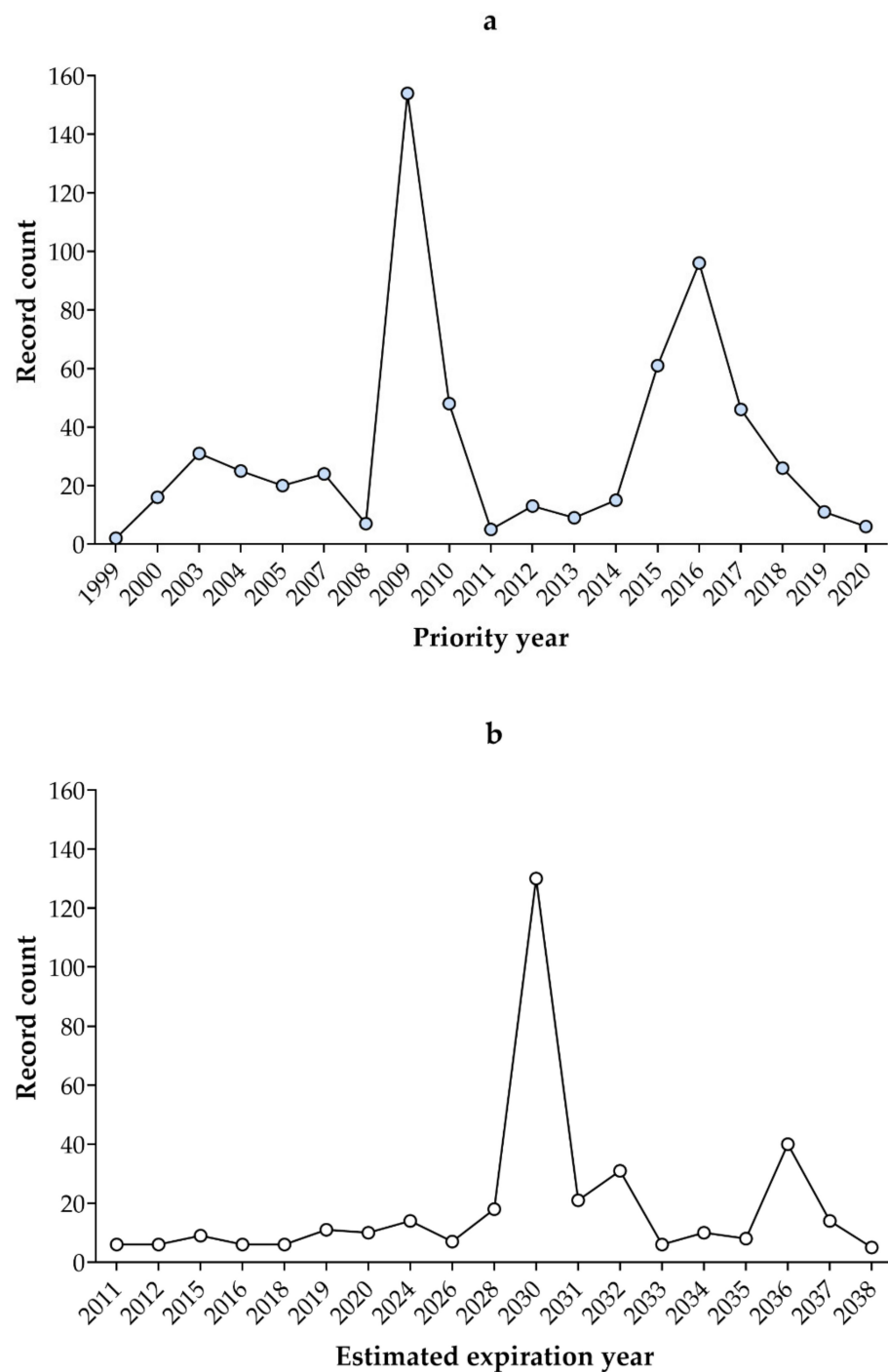
### 3. Results and Discussion

The use of patents is an important tool in the analysis of technologies and innovative activities. In this study, this tool was used to evaluate the technology of interest: chambers for disinfection or sterilization using  $O_3$  or  $O_{3(aq)}$ . Figure 1 shows the annual distribution of patent applications related to the described technology, and the first applications were found in 1999 (Figure 1a). Applications for patent documents were more significant in 2009, reaching a peak of 154 applications, followed by a peak in 2016 with 96 applications. The evolution of the number of patent applications may be related to the need to promote improvements in the processes of the cleaning and disinfection of environmental surfaces, which have been expanding in several areas, such as health, environment, and food [12]. According to the found results, exponential growth was observed between 2008 and 2009, and between 2014 and 2016 in relation to the number of priority patents related to the proposed theme.

The increase in patent applications may be related to the frequency of reported outbreaks of infectious diseases in the last decade. Recent major outbreaks of highly pathogenic or communicable infectious diseases include plague (Madagascar), diphtheria (Bangladesh), Ebola (West Africa and Democratic Republic of Congo), monkey pox (Nigeria), Zika (South and Central America), Middle East respiratory syndrome (MERS-CoV; Saudi Arabia and Korea), and Lassa fever (LF; Nigeria). In addition to sudden morbidities and mortalities, pandemics, and epidemics cause social, political, and economic disorders [40]. However, they promote the search for preventive and strategic methods to contain the spread of diseases [41].

Documents in these specific years were assessed to identify if they could be related to possible epidemics occurred in these periods. In 2009, several countries suffered from the H1N1-related pandemic, at that time still known as swine flu. The global outbreak was characterized by a variant of swine flu of which the first cases occurred in Mexico in mid-March 2009 [42]. In addition to this, other situations could be highlighted, such as outbreaks related to avian influenza in the same year. The second and third years of the greatest observed deposits, 2015 and 2016, were significant for the infection of another world-infamous coronavirus, MERS-CoV [43]. Moreover, the epidemic associated with Zika virus infection greatly impacted mainly South American countries, later being associated to cases of microcephaly and Guillain–Barré syndrome [44,45].

Despite not presenting the specific focus related to these and other cited emergencies in their scope, the vast majority of the developed technologies in the found patent documents focused on applications in health. Patent US007563329B2 (2009) refers to methodology for monitoring the cleaning processes of medical instruments involving a cleaning chamber [46]. Patent US007582257B2 (2009) refers to improvement in the method of the sterilization of medical articles in an  $O_{3(g)}$  humidification chamber [47]. Patent US 20090011044A1 is a technology based on packaging containing sanitizing agent  $O_{3(g)}$  used in the transport of products that need to be kept free from decontamination [48]. Another example, patent US009474815B2 (2016), refers to a method of sequential sterilization aimed at article sterilization based on the action of a conditioning agent and then a sterilizing agent, hydrogen peroxide, and  $O_{3(g)}$ , respectively [49].



**Figure 1.** Temporal analysis of number of patents. (a) evolution per priority year; (b) estimated year for patent expiration.

Cleaning and disinfection processes in this area are important since the use of disinfectant solutions in environmental and surface decontamination is, in a certain way, one of the actions required in the fight against infections due to the growing increase in multiresistant microorganisms to treatments with antimicrobials, associated with high rates of nosocomial infections [13]. This is because, through diverse surfaces (which include articles, medical instrumentation, and equipment), contamination by pathogens can also occur within these environments.

The use of  $O_3$  in the development of these technologies to promote decontamination or sterilization processes can be understood because of its powerful oxidizing action.



When it decomposes, this gas generates an oxidizing reaction by the release of free radicals (ROS), including generating hydroxyl radical (OH<sup>•</sup>), which has greater oxidative potential (2.83 volts) than that of O<sub>3</sub>; and both act on the inactivation of bacteria, fungi, viruses, and protozoa [50–52]. O<sub>3</sub> is an effective and practical antibacterial agent, useful for the inactivation of bacteria of medical importance. Studies showed that a single topical application by nebulization with a low dose of O<sub>3(g)</sub> completely inhibits the growth of potentially pathogenic bacterial strains with known resistance to antimicrobial agents, such as oxacillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus faecalis*, broad spectrum beta-lactamase-producing *Klebsiella pneumoniae*, and carbapenem-resistant *Acinetobacter baumannii* [51]. Sharman and Hudson [53] demonstrated that O<sub>3(g)</sub> at 25 ppm with a short exposure of 20 min and relative humidity of 90% is a bactericide for bacterial strains that commonly cause nosocomial infections. The biocide effect of O<sub>3</sub>, according to Kowalski et al. [54], is very similar in both gaseous and aqueous forms.

In fungi, studies using O<sub>3(g)</sub> and ozonized oil were performed with genera *Epidermophyton*, *Microsporum*, and *Trichophyton*. Results showed that ozonized oil was more efficacious than O<sub>3(g)</sub> is, acting through an oxidative mechanism in cell membranes and revealing their fungicidal effects causing an increase in the evasion of sugar and electrolytes, an effect upon hydrolytic enzymes (such as amylase, lipase, and alkaline phosphatase), and inhibition of sporulation [55].

Regarding viruses, the scientific literature suggested that inactivation by O<sub>3</sub> happens mainly by lipid and protein peroxidation [56–58]. Moreover, O<sub>3</sub> can inactivate viruses, damaging their genetic material, both DNA and RNA [56,59]. The efficacy of O<sub>3</sub> against a variety of simple and complex viruses was demonstrated, including those enveloped and without envelope of DNA and RNA [56,60,61]. Some viruses were more susceptible to the inactivation of O<sub>3(aq)</sub> in short contact time. In about 1 min, 99% of inactivation occurred [35]. In addition, O<sub>3(g)</sub> is highly effective in inactivating the SARS virus with a rate of no less than 99% [56,62].

Table 2 shows examples of studies that evaluated the effectiveness of O<sub>3</sub> use against microorganisms.

**Table 2.** Applications and effectiveness of antimicrobial activity of O<sub>3</sub>.

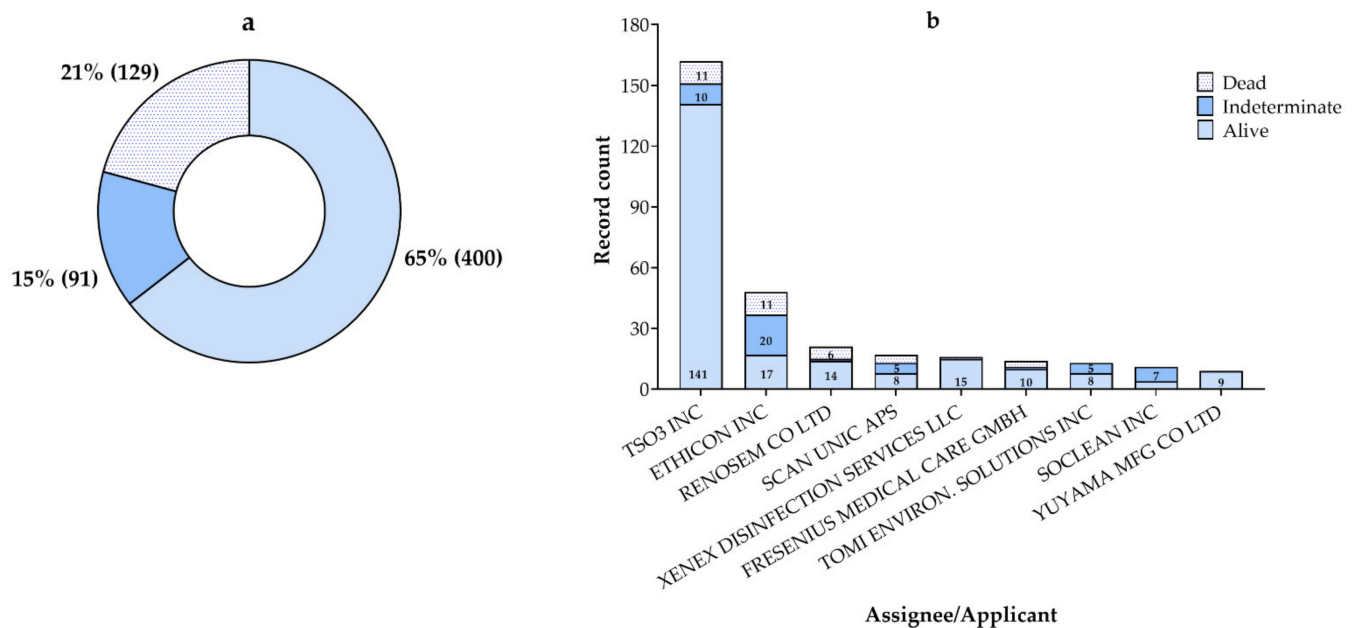
Application	Concentration	Microorganisms	Reference
<b>Virus</b>			
O <sub>3(g)</sub>	1 and 6 ppm	SARS-CoV-2	[29]
O <sub>3(g)</sub>	27.73 ppm	SARS-CoV-1	[31]
O <sub>3(g)</sub>	20–25 ppm	MCoV (murine coronavirus)	[61]
O <sub>3(g)</sub>	0.02–0.05 ppm	Herpes simplex virus 1 (HSV-1)	[63]
		Bovine herpes virus 1 (BoHV1)	
O <sub>3(aq)</sub>	3 and 5 ppm	Murine norovirus (MNV-1)	[64]
O <sub>3(aq)</sub>	1.44 mg/L	Hepatitis A virus (HAV)	[65]
		Poliovirus Type 1	
<b>Bacteria</b>			
O <sub>3(aq)</sub>	0.4 and 0.8 ppm	<i>Escherichia coli</i>	[32]
		<i>Pseudomonas aeruginosa</i> ATCC 15442	
O <sub>3(aq)</sub>	1.2–3.6 µg/mL	<i>Staphylococcus aureus</i> ATCC 6538	[66]
		<i>Escherichia coli</i> NCTC 10538	
		<i>Enterococcus hirae</i> ATCC 1054	
		<i>Streptococcus</i> spp.	
		<i>Staphylococcus aureus</i>	
		<i>Staphylococcus epidermidis</i>	
O <sub>3(g)</sub>	3–3.5 ppm	<i>Aerococcus viridans</i>	[67]
		<i>Enterococcus faecalis</i>	
		<i>Enterococcus faecium</i>	
		<i>Lactobacillus</i> sp.	
		<i>Escherichia coli</i>	
		<i>Pseudomonas aeruginosa</i>	
<b>Fungi</b>			
O <sub>3(g)</sub>	0.5–20 µg/mL	<i>Microsporum canis</i>	[55]
		<i>Microsporum gypseum</i>	
		<i>Trichophyton rubrum</i>	
		<i>Trichophyton interdigitale</i>	
O <sub>3(g)</sub>	2100 ppm/min	<i>Candida albicans</i>	[68]
O <sub>3(aq)</sub>	4 mg/mL	<i>Candida albicans</i>	[68]
O <sub>3(aq)</sub>	1.5–3 µg/mL	<i>Aspergillus brasiliensis</i> ATCC 16404	[68]

Figure 1b presents the expiry year of patent applications according to the protection period of each country. According to the results, documents should expire between 2028 and 2030 according to the legal validity related to invention patents, which usually last 20 years [69]. The largest number of documents with loss of exclusivity are in 2030, which means that the developed technology will enter the public domain and could be reproduced by other companies or institutions in the market in which they were valid. After 2038, a total of 262 documents will expire. These results are in line with the first patent application in 2009, which may be indicative that most patented technologies consist of invention patents that have a protection period of 20 years from the deposit date of the patent. The period of the validity of a patent, whether invention or utility model, may vary according to industrial property laws of each country. In Brazil, for example, it is possible to obtain a technology patent letter in both forms: invention patents with validity of 20 years or utility model patents with validity of 15 years [70].

In many sectors, serious losses in sales and profits for established companies and a drop in productivity in R&D follow the loss of patent protected exclusivity. However, the expiry of patent protection promotes participation and competitiveness among manufacturers of the product in the market, reduction of prices because of increased competition and innovation for the development of new products related to the area of disinfection technologies that use  $O_{3(g)}$  or  $O_{3(aq)}$  as a decontaminating agent [71].

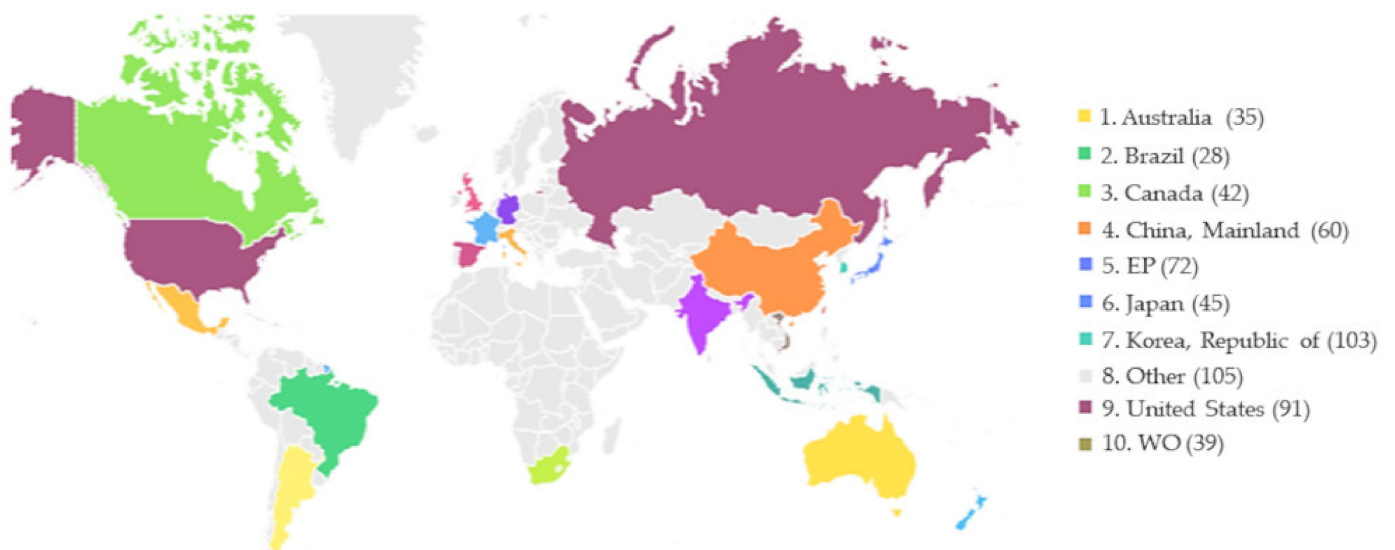
Analysis of the holders and their legal status (Figure 2) showed that 65% of the found patent applications are live patents (400), while 21% are in an undetermined state (129), and 15% are dead (91), totaling the 620 individual documents found in the technological search (Figure 2a). These results indicate the potential development of technologies based on the creation of devices that use  $O_{3(g)}$  or  $O_{3(aq)}$  as a biocide agent for sterilization and disinfection in several areas. The company TSO<sub>3</sub> Inc. has a higher number of current records (141; Figure 2b), comparatively, almost a monopoly of technologies possibly related to  $O_3$  disinfection chambers. These results indicate that this company has 238% more records than its nearest competitor, Ethicon Inc. Although TSO<sub>3</sub> Inc. has some dead records, the number of living records is much higher. In comparison to the top 10 applicants in this set of results, TSO<sub>3</sub> Inc. has 51% of these applicants. Founded in 1998, TSO<sub>3</sub> Inc. covers the sale, production, maintenance, research, development, and licensing of sterilization processes, and related consumable supplies and accessories for heat-sensitive medical devices. The company designs products for sterile processing areas in hospital environments, offering low-temperature sterilization products for hospitals and outpatient surgical centers [72]. According to information generated by the database used in this search (DWPI) on the distribution of the number of patent applications by companies, TSO<sub>3</sub> Inc. filed several applications in the last 20 years, varying in number and having presented a peak in 2013, and always maintained a constant production of patentable technologies, with applications of at least 10 patents between 2013 and 2019. Some companies have documents with diversified legal status, i.e., patents alive (pending, granted), dead (expired, revoked, lapsed), or indeterminate.

The second depositor company is Ethicon Inc., a Johnson and Johnson subsidiary that develops, manufactures, and markets sutures, bandages, staplers, and other wound-closure products [73]. This company went from a lower number of patents filed from 2006 to 2009, to 32 patent applications in 2018. The third depositor, Renosem Co. Ltd., is a supplier of low-temperature plasma sterilizers that aims to ensure infection prevention and microbial reduction. In addition, it develops several medical devices using high-tech plasma applications [74]. Renosem's contribution in patent filings related to technologies involving  $O_3$  occurred mostly between 2007 and 2013. Yuyama Mfg Co. only has dead patents (9).



**Figure 2.** Analysis of number of patent documents. (a) general legal status of the publications found; (b) number of publications per applicant.

The main countries and regions of deposit of this type of technology are demonstrated in Figure 3. This result usually highlights the main protection sites of technologies related to disinfection chambers using  $O_{3(g)}$  or  $O_{3(aq)}$ . South Korea and United States have the largest number of patent applications, with a total of 103 and 91 applications, respectively.



**Figure 3.** Geographical distribution of patent applications related to  $O_{3(g)}$  or  $O_{3(aq)}$  disinfection devices or chambers; European Patent Office (EP), WO (or World Intellectual Property Organization (WIPO)).



From Korea, patent number KR1863560B1 deals with a sterilization chamber for medical equipment with support for supplying  $O_{3(g)}$  to a reaction chamber; patent number KR2012093790A can also be used in healthcare, highlighting that both  $O_{3(g)}$  and hydrogen peroxide are used in a mixture for sanitization. Many patent applications by the country are filed in the United States, which corroborates other outcomes found in this technological assessment, indicating that the United States is the largest market for the development of these inventions, and the most active in technological development. Thus, examples include documents no. US10660980B2 (sanitation system using  $O_{3(g)}$  for cleaning, disinfection, and sterilization of various objects such as medical devices. It comprises an  $O_3$ -generating device coupled with a container to receive  $O_{3(g)}$  to sanitize objects), US10632220B2 (medical-device sterilization cabinet as endoscope), and US10632218B2 (method for the continuous debacterization of solid food products that involves transporting the product through the entrance of the chamber in continuous motion, so that the product is continuously exposed to the  $O_3$  atmosphere inside the chamber).

Other countries were identified related to these results: China received 60 orders, Canada 42, and Japan 45 requests for deposits. At least two international organizations were identified, namely, the European Patent Office (EPO) and World Intellectual Property Organization (WIPO) with 72 and 39 applications, respectively. Through these organizations, several international applications can be made through a single application, such as the WIPO Patent Cooperation Treaty (PCT) [75]. Most of those responsible for the technologies seek to protect their inventions through international requests via the EPO and WIPO in order to reduce costs and simplify the process of individual deposits in each country, simultaneously protecting their technology in several countries [76].

In South America, Brazil stands out with 28 deposits referring to this type of technology, and it has its publications focused on the sterilization of medical devices, pharmaceutical products, surgical instruments, and articles in general. The difference and perhaps the technology that most resembles the proposed use as a barrier for individuals, is in BR112017015030A2, which deals with a device for hand sanitization, with an  $O_{3(aq)}$  outlet with distribution openings that allow for the spread of water over the palm and back of the hands.

Table 3 shows some documents found in this prospecting.

**Table 3.** Examples of recent documents found in technological prospection.

Title	Application Number	Assignee or Inventor	Deposited Country	Related To
Disinfecting articles with O <sub>3</sub>	US15877036A	Éclair Medical Systems Inc.	United States	Methods, apparatus, and systems for disinfecting articles with O <sub>3(g)</sub> . Involves sterilization chamber for medical articles that are confined and sealed, so as to not interact with external atmosphere. O <sub>3</sub> concentrations are applied until complete material disinfection or sterilization [77].
Devices for disinfection, deodorization, and/or sterilization of objects	US15533653A	Microlin LLC	United States	Treatment chamber in which an object can be disinfected, deodorized, and/or sterilized (e.g., endoscope components). Includes nebulizer, Fenton generator, and hydrogen peroxide in presence of nanoparticle catalyst and UV light, and O <sub>3(g)</sub> can be applied as additional treatment agent [78].
O <sub>3</sub> Sterilization Device	KR201646115A	Hu, P.K and Young, L	South Korea	O <sub>3(g)</sub> sterilization device for medical devices comprising container, control box, sterile room, discharge tube, connection pipe, air compressor, and neutralization [79].
Sterile environment maintenance method of operation chamber, sterile environment maintenance device	CN202010309498A	Yushinomi Electric Co.	China	Method for maintaining sterile environment of working chambers. Process generates O <sub>3</sub> from wavelength-long violet rays, introducing O <sub>3(g)</sub> into the chamber, and breaking down introduced O <sub>3</sub> into oxygen radicals [80].
Method for sterilization of an article in a sealable sterilization chamber	BR12201310297A	TSO <sub>3</sub> INC.	Brazil	Sterilization method and device containing hydrogen peroxide or O <sub>3(g)</sub> as sterilizing agent for sterilization of medical articles or instruments (e.g., gastroscopes and colonoscopes) in sealable sterilization chamber [81].
Apparatus, method and software product for hand sanitization by application of ozonated water	BR112017015030A2	SCAN UNIC APS	Brazil	Disinfection chamber that comprises ozone water output of ozone water supply for delivery of O <sub>3(aq)</sub> to hands when inserted into the apparatus.

The prospected documents in this study did not have a specific focus on the control of emergency infections. However, a great majority of the developed technologies through chambers or methods of disinfection with the use of  $O_{3(g)}$  or  $O_{3(aq)}$  are directed to health applications for processes of pathogen decontamination. These technologies could be applied for the control of emergency diseases (or at least the method by which they act), for example, COVID-19. Tunnels, cabs, or disinfecting chambers gained popularity because they represent an efficient option for surface disinfection since the disinfecting agent is dispersed by means of a spraying system, and can thus act in large and complex areas in a short amount of time [19]. Thus, its application was directed to environments with great circulation of people, such as industries [24], and has gained more attention due to the potential for microorganism transmission, such as SARS-CoV-2. There are some companies in the market that already sell cabins, tunnels, and cameras coupled to an  $O_3$  generator for the disinfection of people, clothing, or equipment, and some are already previously installed in public environments (examples are shown in Table 4). Nevertheless, no information is shown regarding the stability of the obtained product, or technical reports that guarantee efficacy for a reduction in general microbial load on different surfaces and over an adequate amount of time after exposure to the biocide agent; therefore, the efficacy of these structures has not been clarified to date, which generates doubts for supervising sanitary agencies regarding the real applicability of these products.

**Table 4.** Companies and institutions that produce cabins, chambers, and disinfection tunnels coupled with  $O_3$  generator.

Company/Institution	Product	Country of Origin	Reference
Genial Medical	Disinfection Tunnel Anti-COVID-19	China	[82]
Broad Group Ltd.	BROAD Disinfection Cabin	China	[83]
myOzone	Ozone Mist Disinfectant Tunnel	Brazil	[84]
Federal Technological University of Paraná	Wet ozone disinfection booth	Brazil	[85]
Tropical Clean	Tropical Clean-Individual Disinfection System	Brazil	[86]
Eurobras	Ozonized Disinfection Chamber	Brazil	[87]
B <sub>3</sub> Zonio	Individual Body Disinfection Cabin	Brazil	[88]
OZ-AIR®	$O_3$ -based sterilization tunnel	India	[89]
SafeWay	Disinfection cabin	United States	[90]

In terms of scientific publications, some studies approached the use of disinfection chambers and tunnels not only via  $O_{3(g)}$  or  $O_{3(aq)}$ . Maurya et al. [22] developed one that is used for the disinfection of people's body with the application of a disinfection solution and far-ultraviolet C. This aims at reducing viral contamination on clothing, skin, and any other exposed surface. This and other studies are summarized in Table 5.

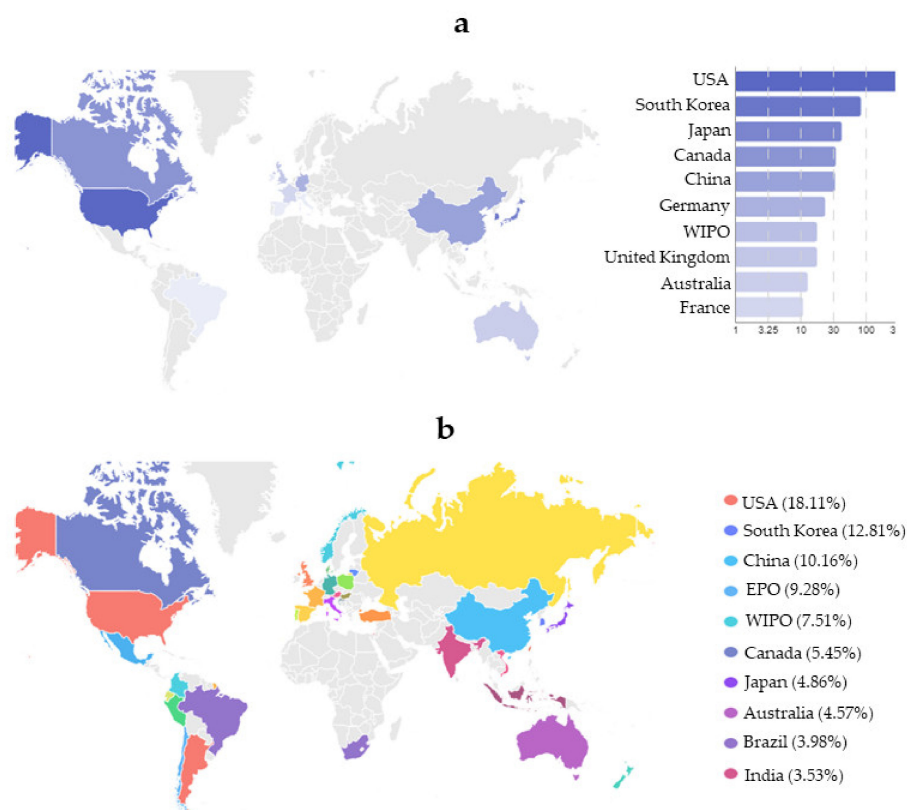
These findings, together with the number of documents that address  $O_3$ -based disinfection technologies, indicate that the use of disinfection chambers or similar structures to carry out disinfection processes against pathogens is promising, especially when it comes to their health application, whether for the disinfection of medical articles or for utensils, protective equipment, and others. However, regarding use as a protection barrier for individuals, no considerable number of studies and patent applications were found that could better substantiate this type of application.

Some countries stand out in relation to the choice of applicants for the request for initial protection. Figure 4a shows the relevant countries and regions. According to the generated data in the research base, 4% of the companies seek protection in the four largest markets: the United States, South Korea, Japan, and Canada. This shows a compromised investment of the countries and a wider market for these inventions. In general, 10% of the companies are entering orders in more than four countries. A global archiving strategy can demonstrate a greater market potential in this space. In the analysis of potential markets for deposit of this type of technology (Figure 4b), it makes sense that the United States and

South Korea are the main markets for deposit and search of protection after deposit in the countries of origin since they are the most promising markets for the development of this type of technology.

**Table 5.** Articles that focus on the use of disinfection chambers.

Title	Main Findings and/or Conclusions	Reference
Development of Autonomous Advanced Disinfection Tunnel to Tackle External-Surface Disinfection of COVID-19 Virus in Public Places	The technology is based on a disinfection tunnel to disinfect external surfaces of COVID-19 such as clothes and open body sections in public places such as airports, office complexes, schools, and malls. It is based on the use of two chambers: the first sprays a mist of herbal disinfectant solution or sodium hypochlorite solution, and the second is hot-air and far-ultraviolet C (far-UVC).	[22]
UVC LED Irradiation Effectively Inactivates Aerosolized Viruses, Bacteria, and Fungi in a Chamber-Type Air Disinfection System	Evaluation of air disinfection using a disinfection chamber using a set of UVC light-emitting diodes (LED) against microorganisms. Results showed efficacy in viral inactivation, such as MS2 bacteriophage, and against bacteria (e.g., <i>Salmonella enterica</i> serovar Typhimurium) and fungi (e.g., <i>Aspergillus flavus</i> ).	[91]
Construction of Its Evaluation System in Originally Designed Test-Chamber System and Sporicidal Activity of Aerosolized Hypochlorite Solution to <i>Bacillus subtilis</i> Spores	Disinfection chamber using a 5% sodium hypochlorite solution-spraying system. Results demonstrated efficacy in the inactivation of <i>Bacillus subtilis</i> spores in the process of decontaminating small surface areas.	[19]
Disinfection efficiency of positive pressure respiratory protective hood using fumigation sterilization cabinet	Fumigation cabinet based on hydrogen peroxide for the disinfection of positive pressure respiratory protective hoods (PPRPH) to allow for the safe reuse of protective equipment. Results showed effectiveness in the decontamination process against <i>Geobacillus stearothermophilus</i> . Besides bacterial inactivation being effective, the physical and chemical properties of the equipment were maintained.	[92]



**Figure 4.** Geographical distribution in relation to (a) main countries of initial search for protection of the prospected technologies, and (b) potential markets for deposit of this type of technology.

The United States is a powerhouse in the development of solutions in several areas, including surface disinfection, probably because of the promotion of a competitive scenario with the participation of multinational companies, which increases the demand for the development of these technologies [93]. This may be one of the reasons why it is one of the preferred markets for the protection of technologies developed by other countries. Given that they are world powers, it is expected that competitors want to protect their technologies in the United States before it is developed in the country.

In analysis performed by the DWPI database in relation to this result, 45% of the global requests in these results are granted, which indicates the protection for active patents (alive) in the relevant markers, and 55% of this set of results are pending as requests. To better understand the results, countries or organizations with higher percentages point to new or growing markets, while those with lower order rates may indicate established markets or areas of low growth. The United States, South Korea, and China are at 18.11%, 12.81%, and 10.16%, respectively, so they are the most promising markets and in greater competition in relation to the development of disinfection chambers with the use of  $O_{3(g)}$  or  $O_{3(aq)}$ .

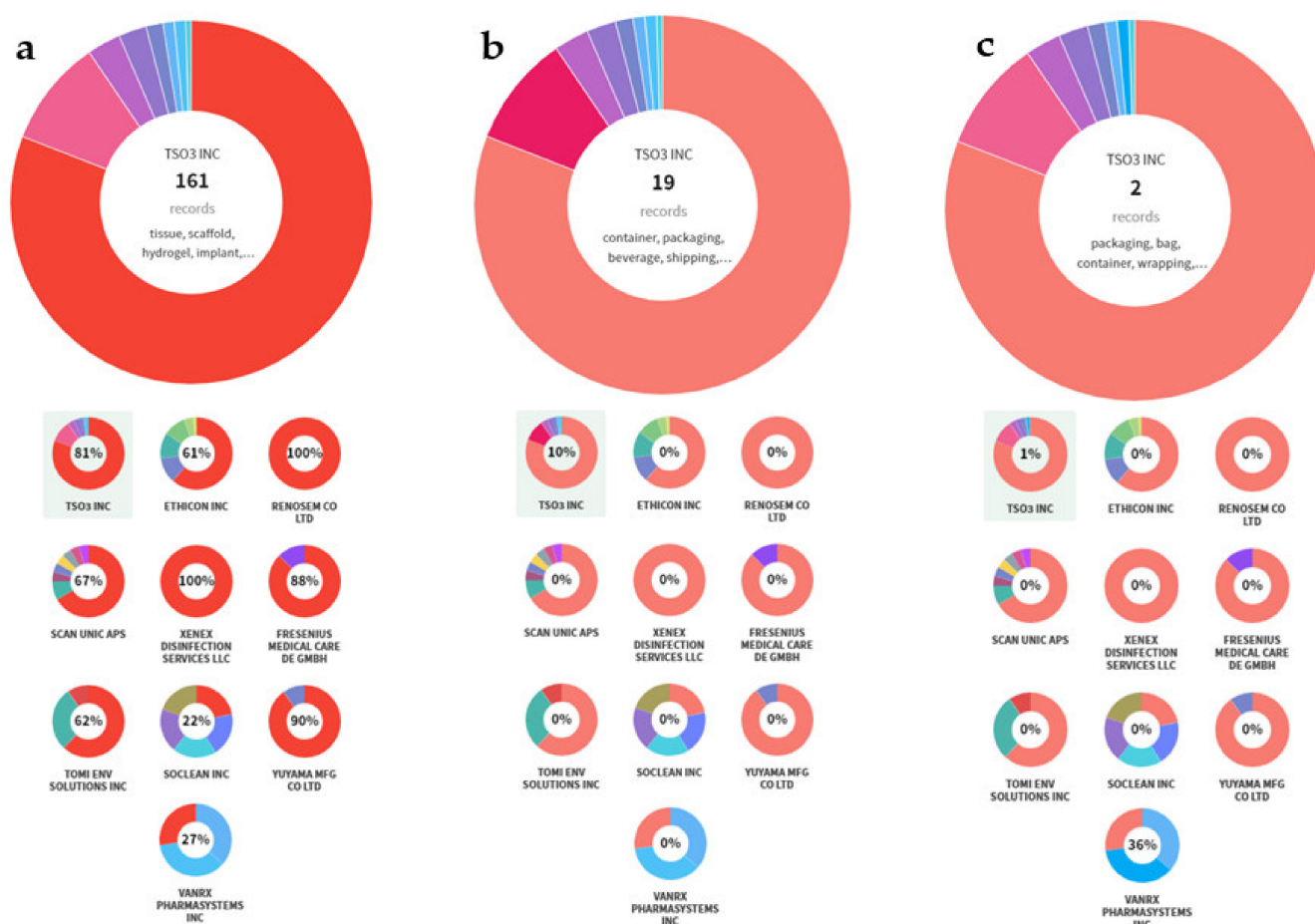
In the case of Brazil, which consists in 3.98% of deposits, only one patent application was from a Brazilian company (Futura Industrial e Comercial LTDA). The document refers to a utility model of a sterilization and deodorization cabin that uses  $O_{3(g)}$ . The purpose of the system is the general sanitization of garments and objects. The remaining percentage consists of applications made by companies from other countries, mainly by TSO<sub>3</sub> Inc., Canada. Other examples of depositing countries in Brazil are Denmark, the United States, and Germany.

In analyzing the main dominant areas to which the prospected technology is directed (Figure 5), the three main categories were selected (among 20 found) according to the percentage of development by the main applicants (TSO<sub>3</sub> Inc., Québec, QC, Canada). The technologies were: (a) tissue, scaffold, hydrogel, implant, medical, dressing, collagen; (b) container, packaging, beverage, shipping, pallet, lid, bag; (c) packaging, bag, container, wrapping, filling, blister, packing. Technologies (a) and (b) were found in 94% of the patent documents. High percentages of the technologies of interest demonstrate technological saturation in this area, while small percentages point to diverse technological representation. This same year presented itself as the most significant in relation to technological diversity, with over 63% representation of all found technologies.

Of TSO<sub>3</sub> Inc. patent applications, 81% refer to main technology (a). According to database analysis, this technology presented a peak in 2018 with an average of three registers per year. Concerning other applicants, all documents (100%) of Renosem Co. Ltd. and Xenex Disinfection Services LCC are in this technological area, while SoClean Inc. had the lowest percentage (22%). Analyzing technology (b), only TSO<sub>3</sub> Inc. had patent applications in this area, but only 10% corresponded to this technology. Lastly, in relation to technology (c), the representativity of TSO<sub>3</sub> Inc. loses space to Vanrx Pharmsystems Inc., with the highest percentage of applications in this area (36%).

In the evaluation of classifications through CPC codes found in the documents (Figure 6), two of the codes used in the prospection (A61L2/202—ozone (gas); A61L2202/122—chambers for sterilization) were the most found, displaying a total of 501 and 493 records, respectively. The third most-used code (A61L2202/14) is specific to means to control sterilization processes, data processing, presentation and storage means, being present in 354 records. Code A61L2202/24 (medical instruments, e.g., endoscopes, catheters, perforators) was the fourth most-used in 328 records. The presence of these codes demonstrates that the disinfection of surfaces and instruments is being protected in the great majority of documents. Table 6 shows the description of the CPC codes in the records.

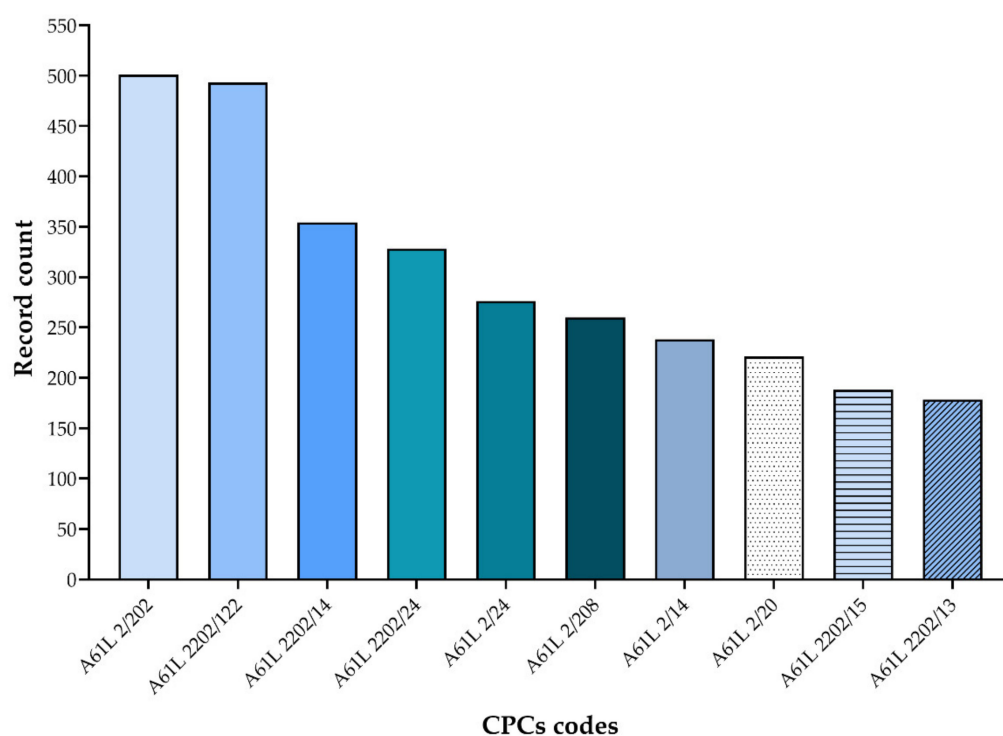




**Figure 5.** Analysis of top technological areas related to patent documents referring to disinfection chambers using  $O_{3(g)}$  or  $O_{3(aq)}$ . Comparisons between top filing company TSO<sub>3</sub> Inc. and other companies were performed for three types of technologies. (red) Technology (a) highlighting number of patents applications by TSO<sub>3</sub> Inc. (161), center of the donut chart. Percentage values of other companies (also in red) compared to this number shown in the smaller donut charts below. Other colors are related to other, not shown technologies. Same analysis was applied to technologies (b,c).

**Table 6.** CPC codes in technological prospecting.

CPC Code	Related To
A61L2/202	Ozone (gas)
A61L 2202/122	Chambers for sterilization
A61L 2202/14	Means for controlling sterilization processes, data processing, presentation and storage means, e.g., sensors, controllers, programs
A61L 2202/24	Medical instruments, e.g., endoscopes, catheters, sharps
A61L 2/24	Apparatus using programmed or automatic operation
A61L 2/208	Hydrogen peroxide
A61L 2/14	Plasma, i.e., ionized gases
A 61L 2/20	Gaseous substances, e.g., vapors
A61L 2202/15	Biocide distribution means, e.g., nozzles, pumps, manifolds, fans, baffles, sprayers
A61L 2202/13	Biocide decomposition means, e.g., catalysts, sorbent



**Figure 6.** Most-used classification codes in area of development of disinfection devices and cameras with use of  $O_{3(g)}$  or  $O_{3(aq)}$ .

Surprisingly, the other code used in the search strategy (A61L2/183—ozone dissolved in liquid), was not among the 10 most used codes. Since this code was used in the search strategy for the documents, however, in the results it was not present among the 10 most used codes, it may be an indication that the number of applications involving disinfection chamber technologies using  $O_{3(aq)}$  must be low. Furthermore, it may be an indication that there should be more intense focus by research centers and companies on the development of sterilization processes using  $O_{3(g)}$ , since it is a safe, fast, and economical alternative when compared to other low-temperature sterilization methods for the disinfection and/or sterilization of medical devices and environments. Thus, the application of  $O_{3(aq)}$  becomes a field of opportunity to be explored regarding the applications of disinfection measures. In addition, these findings highlight inventiveness and a promising area for inventions related to the use of this technology as a human protection barrier. Furthermore, the presence of these codes demonstrates the surface- and instrument-disinfectant character of the great majority of documents. This highlights the main protected technologies in the set of documents, showing the distribution of the main codes in this particular portfolio of patents, and may help to identify thematic areas in which new technologies, such as the development of disinfection chambers that can be used safely by people, can be developed.

#### 4. Conclusions

Research into new technologies linked to the development of disinfection chambers using  $O_{3(g)}$  or  $O_{3(aq)}$  as a decontamination agent is increasingly evolving, mostly driven by the COVID-19 pandemic. In the 620 documents found in this prospection, none of the technologies observed had its use directed to the protection of individuals; the majority was instead directed to the sterilization or decontamination of medical devices and surfaces. Furthermore, the absence of the specific CPC code for  $O_3$  dissolved in liquid indicated the innovation potential that could be used as a barrier to protect individuals, using  $O_{3(aq)}$  as sanitizer. Nevertheless, inventions based on this type of development must be duly scientific in order to guarantee the effectiveness of this decontaminating agent against several pathogens, including SARS-CoV-2, without disregarding safe use.

**Author Contributions:** Conceptualization: L.A.B.M., A.Á.B.S., G.A.F.M., G.M.L., C.N., M.G. and B.A.S.M.; formal analysis: L.A.B.M., F.O.O., E.S.d.S., L.M.C.d.S., L.d.A.P.R., P.R.F.N. and B.A.S.M.; funding acquisition: L.A.B.M., G.A.F.M., G.M.L. and B.A.S.M.; investigation: P.R.F.N., A.Á.B.S., C.N. and B.A.S.M.; methodology: F.O.O., E.S.d.S., L.M.C.d.S., L.d.A.P.R. and B.A.S.M.; project administration: A.Á.B.S., G.A.F.M., G.M.L., M.G. and B.A.S.M.; resources: C.N. and M.G.; software: F.O.O., E.S.d.S., L.M.C.d.S. and L.d.A.P.R.; supervision: L.A.B.M., G.A.F.M. and B.A.S.M.; validation: A.Á.B.S. and G.M.L.; writing—original draft: L.A.B.M., F.O.O., E.S.d.S., L.M.C.d.S., L.d.A.P.R., P.R.F.N., A.Á.B.S., G.A.F.M., G.M.L., C.N., M.G. and B.A.S.M. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research was funded by China Three Gorges Corporation—CTG BRASIL (Rio Paraná Energia S.A. Rodovia MS-444 s/n° km 58, Ilha Solteira, Selviria 79590-000, MS), with resources for the ANEEL R&D Program (PD-10381-0420/2020) and SENAI CIMATEC.

**Institutional Review Board Statement:** Not applicable.

**Informed Consent Statement:** Not applicable.

**Data Availability Statement:** Data is contained within the article.

**Acknowledgments:** The authors greatly thank the University Center SENAI/CIMATEC (National Service for Industrial Training—Serviço Nacional de Aprendizagem Industrial)—SENAI CIMATEC (Bahia—Brazil) and to China Three Gorges Corporation—CTG Brazil.

**Conflicts of Interest:** The authors declare no conflict of interest.

## References

1. van Doorn, H.R. Emerging infectious diseases. *Medicine* **2014**, *42*, 60–63. [\[CrossRef\]](#)
2. McMichael, A.J. Environmental and social influences on emerging infectious diseases: Past, present and future. *Philos. Trans. R. Soc. Lond. Ser. B Biol. Sci.* **2004**, *359*, 1049–1058. [\[CrossRef\]](#)
3. Pan, J.; St. Pierre, J.M.; Pickering, T.A.; Demirjian, N.L.; Fields, B.K.K.; Desai, B.; Gholamrezaezhad, A. Coronavirus disease 2019 (COVID-19): A modeling study of factors driving variation in case fatality rate by country. *Int. J. Environ. Res. Public Health* **2020**, *17*, 8189. [\[CrossRef\]](#) [\[PubMed\]](#)
4. Li, Q.; Guan, X.; Wu, P.; Wang, X.; Zhou, L.; Tong, Y.; Ren, R.; Leung, K.S.M.; Lau, E.H.Y.; Wong, J.Y.; et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N. Engl. J. Med.* **2020**, *382*, 1199–1207. [\[CrossRef\]](#) [\[PubMed\]](#)
5. Zhu, N.; Zhang, D.; Wang, W.; Li, X.; Yang, B.; Song, J.; Zhao, X.; Huang, B.; Shi, W.; Lu, R.; et al. A novel coronavirus from patients with pneumonia in China. *N. Engl. J. Med.* **2020**, *382*, 727–733. [\[CrossRef\]](#) [\[PubMed\]](#)
6. Bani Younes, A.; Hasan, Z. COVID-19: Modeling, Prediction, and Control. *Appl. Sci.* **2020**, *10*, 3666. [\[CrossRef\]](#)
7. Huang, C.; Wang, Y.; Li, X.; Ren, L.; Zhao, J.; Hu, Y.; Zhang, L.; Fan, G.; Xu, J.; Gu, X.; et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* **2020**, *395*, 497–506. [\[CrossRef\]](#)
8. Kratzel, A.; Todt, D.; V'kovski, P.; Steiner, S.; Gultom, M.; Thao, T.T.N.; Ebert, N.; Holwerda, M.; Steinmann, J.; Niemeyer, D.; et al. Inactivation of Severe Acute Respiratory Syndrome Coronavirus 2 by WHO-Recommended Hand Rub Formulations and Alcohols. *Emerg. Infect. Dis.* **2020**, *26*, 1592–1595. [\[CrossRef\]](#) [\[PubMed\]](#)
9. Donskey, C.J. Decontamination devices in health care facilities: Practical issues and emerging applications. *Am. J. Infect. Control* **2019**, *47*, A23–A28. [\[CrossRef\]](#) [\[PubMed\]](#)
10. Weber, D.J.; Kanamori, H.; Rutala, W.A. 'No touch' technologies for environmental decontamination. *Curr. Opin. Infect. Dis.* **2016**, *29*, 424–431. [\[CrossRef\]](#)
11. Kchaou, M.; Abuhasel, K.; Khadr, M.; Hosni, F.; Alquraish, M. Surface Disinfection to Protect against Microorganisms: Overview of Traditional Methods and Issues of Emergent Nanotechnologies. *Appl. Sci.* **2020**, *10*, 6040. [\[CrossRef\]](#)
12. Bloomfield, S.F. Importance of disinfection as a means of prevention in our changing world hygiene and the home. *GMS Krankenhhyg. Interdiszip.* **2007**, *2*, Doc25. [\[PubMed\]](#)
13. Communication from the Commission to the European Parliament and the Council. In *Action Plan Against the Rising Threats from Antimicrobial Resistance*; European Commission: Brussels, Belgium, 2011; ISBN 9783540773405.
14. Gebel, J.; Exner, M.; French, G.; Chartier, Y.; Christiansen, B.; Gemein, S.; Goroncy-Bernes, P.; Hartemann, P.; Heudorf, U.; Kramer, A.; et al. The role of surface disinfection in infection prevention. *GMS Hyg. Infect. Control* **2013**, *8*, Doc10. [\[CrossRef\]](#) [\[PubMed\]](#)
15. Lauritano, D.; Moreo, G.; Limongelli, L.; Nardone, M.; Carinci, F. Environmental Disinfection Strategies to Prevent Indirect Transmission of SARS-CoV2 in Healthcare Settings. *Appl. Sci.* **2020**, *10*, 6291. [\[CrossRef\]](#)
16. Dellinger, E.P. Prevention of Hospital-Acquired Infections. *Surg. Infect.* **2016**, *17*, 422–426. [\[CrossRef\]](#) [\[PubMed\]](#)
17. Cadnum, J.L.; Jencson, A.L.; Livingston, S.H.; Li, D.F.; Redmond, S.N.; Pearlmutter, B.; Wilson, B.M.; Donskey, C.J. Evaluation of an electrostatic spray disinfectant technology for rapid decontamination of portable equipment and large open areas in the era of SARS-CoV. *Am. J. Infect. Control* **2020**, *48*, 951–954. [\[CrossRef\]](#)

18. Silva, D.F.; Toledo Neto, J.L.; Machado, M.F.; Bochnia, J.R.; Garcez, A.S.; Foggiano, A.A. Effect of photodynamic therapy potentiated by ultrasonic chamber on decontamination of acrylic and titanium surfaces. *Photodiagnosis Photodyn. Ther.* **2019**, *27*, 345–353. [CrossRef] [PubMed]
19. Ishikawa, S.; Ueno, S.; Mitsui, M.; Matsumura, Y.; Hatsuoka, T. Construction of Its Evaluation System in Originally Designed Test-Chamber System and Sporicidal Activity of Aerosolized Hypochlorite Solution to *Bacillus subtilis* Spores. *Biocontrol Sci.* **2019**, *24*, 57–65. [CrossRef] [PubMed]
20. ANVISA—National Health Surveillance Agency. *Technical Note No 51/2020/SEI/COSAN/GHCOS/DIRE3/ANVISA. Disinfection of People in Public Places and Hospitals during the Covid 19 Pandemic*; ANVISA: Brasília, Brazil, 2020; pp. 1–6.
21. Biswal, M.; Kanaujia, R.; Angrup, A.; Ray, P.; Mohan Singh, S. Disinfection tunnels: Potentially counterproductive in the context of a prolonged pandemic of COVID. *Public Health* **2020**, *183*, 48–49. [CrossRef]
22. Maurya, D.; Gohil, M.K.; Sonawane, U.; Kumar, D.; Awasthi, A.; Prajapati, A.K.; Kishnani, K.; Srivastava, J.; Age, A.; Pol, R.; et al. Development of Autonomous Advanced Disinfection Tunnel to Tackle External Surface Disinfection of COVID-19 Virus in Public Places. *Trans. Indian Natl. Acad. Eng.* **2020**, *5*, 281–287. [CrossRef]
23. ANVISA—National Health Surveillance Agency. *Technical Note No 34/2020/SEI/COSAN/GHCOS/DIRE3/ANVISA. Recommendations and Alerts on Disinfection Procedures in Public Places Carried Out during the COVID-19 Pandemic*; ANVISA: Brasília, Brazil, 2020.
24. Wickramatillake, A.; Kurukularatne, C. SARS-CoV-2 human disinfection chambers: A critical analysis. *Occup. Med.* **2020**, *70*, 330–334. [CrossRef]
25. Dev Kumar, G.; Ravishankar, S.; Juneja, V.K. Interventions for Fresh Produce. In *Microbial Control and Food Preservation*; Springer: New York, NY, USA, 2017; pp. 199–223, ISBN 9781493975563.
26. Pruetz, S.B.; Tan, W.; Sebastian, T.; Liu, D. Inflammation and Organ Failure. In *Comprehensive Toxicology*; Elsevier: Amsterdam, The Netherlands, 2010; Volume 5, pp. 299–321, ISBN 9780080468686.
27. Scott, D.B.; Leshner, E.C. Effect of ozone on survival and permeability of *Escherichia coli*. *J. Pathol. Bacteriol.* **1963**, *85*, 567–568. [CrossRef]
28. Dev Kumar, G.; Williams, R.C.; Sumner, S.S.; Eifert, J.D. Effect of ozone and ultraviolet light on *Listeria monocytogenes* populations in fresh and spent chill brines. *Food Control* **2016**, *59*, 172–177. [CrossRef]
29. Yano, H.; Nakano, R.; Suzuki, Y.; Nakano, A.; Kasahara, K.; Hosoi, H. Inactivation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by gaseous ozone treatment. *J. Hosp. Infect.* **2020**, *106*, 837–838. [CrossRef]
30. Blanchard, E.L.; Lawrence, J.D.; Noble, J.A.; Xu, M.; Joo, T.; Ng, N.L.; Schmidt, B.E.; Santangelo, P.J.; Finn, M.G. Enveloped Virus Inactivation on Personal Protective Equipment by Exposure to Ozone. *medRxiv Prepr. Serv. Heal. Sci.* **2020**. [CrossRef]
31. Jia-min, Z.; Chong-yi, Z.; Geng-fu, X.; Yuan-quan, Z.; Rong, G. Examination of the Efficacy of Ozone Solution Disinfectant in Activating Sars Virus. *Chin. J. Disinfect.* **2004**, *21*, 27–28.
32. Breidablik, H.J.; Lysebo, D.E.; Johannessen, L.; Skare, Å.; Andersen, J.R.; Kleiven, O.T. Ozonized water as an alternative to alcohol-based hand disinfection. *J. Hosp. Infect.* **2019**, *102*, 419–424. [CrossRef] [PubMed]
33. Kampf, G.; Todt, D.; Pfaender, S.; Steinmann, E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. *J. Hosp. Infect.* **2020**, *104*, 246–251. [CrossRef] [PubMed]
34. Nakamura, K.; Saito, K.; Kashiwazaki, J.; Aoyagi, T.; Arai, K.; Hara, Y.; Kobari, S.; Mori, H.; Ohashi, K.; Takano, Y.; et al. Evaluation of ozonated water using ASTM E1174 for standardized testing of handwash formulations for healthcare personnel. *J. Hosp. Infect.* **2018**, *100*, 211–213. [CrossRef]
35. Shin, G.-A.; Sobsey, M.D. Reduction of Norwalk Virus, Poliovirus 1, and Bacteriophage MS2 by Ozone Disinfection of Water. *Appl. Environ. Microbiol.* **2003**, *69*, 3975–3978. [CrossRef] [PubMed]
36. Giuroiu, C.L.; Andrian, S.; Stoleriu, S.; Scurtu, M.; Țănculescu, O.; Poroch, V.; Sălceanu, M. The Combination of Diode Laser and Ozonated Water in the Treatment of Complicated Pulp Gangrene. *Appl. Sci.* **2020**, *10*, 4203. [CrossRef]
37. Suchomel, M.; Lenhardt, A.; Kampf, G.; Grisold, A. *Enterococcus hirae*, *Enterococcus faecium* and *Enterococcus faecalis* show different sensitivities to typical biocidal agents used for disinfection. *J. Hosp. Infect.* **2019**, *103*, 435–440. [CrossRef]
38. National Institute of Health. *Transforming Clinical Research in the United States*; National Academies Press (US): Washington, DC, USA, 2010; ISBN 9780309153324.
39. World Health Organization. *Review of Evidence on Health Aspects of Air Pollution—REVIHAAP Project*; WHO: Geneva, Switzerland, 2013.
40. Madhav, N.; Oppenheim, B.; Gallivan, M.; Mulembakani, P.; Rubin, E.; Wolfe, N. Pandemics: Risks, Impacts, and Mitigation. In *Disease Control Priorities, Third Edition (Volume 9): Improving Health and Reducing Poverty*; Jamison, D.T., Gelband, H., Horton, S., Jha, P., Laxminarayan, R., Mock, C.N., Nugent, R., Eds.; The World Bank: Washington, DC, USA, 2017; pp. 315–345, ISBN 9781464805271.
41. Khan, M.H.; Yadav, H. Sanitization During and After COVID-19 Pandemic: A Short Review. *Trans. Indian Natl. Acad. Eng.* **2020**. [CrossRef]
42. Ministry of Health 10 Years Since the Global Outbreak of H1N1. Available online: <http://www.blog.saude.gov.br/index.php/53845-10-anos-do-surto-global-de-h1n1#:~:text=Emabrilde2009%2Ca,mêsde2009> (accessed on 6 December 2020).
43. Giuliani, G.; Ricciuti, G.; Galoforo, A.; Franzini, M. Microbiological aspects of ozone: Bactericidal activity and antibiotic/antimicrobial resistance in bacterial strains treated with ozone. *Ozone Ther.* **2018**, *3*, 1573–1580. [CrossRef]
44. World Health Organization Emergencies Preparedness, Response: Diseases. Available online: [https://www.who.int/csr/disease/swineflu/frequently\\_asked\\_questions/pandemic/en/](https://www.who.int/csr/disease/swineflu/frequently_asked_questions/pandemic/en/) (accessed on 6 December 2020).



45. Ministry of Health. *Zika Virus in Brazil*; Secretariat of Health Surveillance: Brasília, Brazil, 2017; ISBN 9788533424821.
46. Lin, S.-M.; Jacobs, P.T.; Wang, J.-H.; Platt, R.C.; Zhu, P.C. *Monitoring of Cleaning Process*; Ethicon Inc.: Cornelia, GA, USA, 2009.
47. Bedard, C.; Dufresne, S.; Leblond, H.; Martel, C.; Martel, K. *Ozone Sterilization Method*; TSO<sub>3</sub> Inc.: Québec, QC, Canada, 2009.
48. Gutman, J. Ozone Containing Product Package. U.S. Patent 20090011044, 8 January 2009.
49. Dufresne, S.; Martel, C.; Leblond, H.; Dassie, N.; Martel, K. *Sterilization Method and Apparatus*; TSO<sub>3</sub> Inc.: Québec, QC, Canada, 2016.
50. Megahed, A.; Aldridge, B.; Lowe, J. The microbial killing capacity of aqueous and gaseous ozone on different surfaces contaminated with dairy cattle manure. *PLoS ONE* **2018**, *13*, e0196555. [CrossRef]
51. Fontes, B.; Cattani Heimbecker, A.M.; de Souza Brito, G.; Costa, S.F.; van der Heijden, I.M.; Levin, A.S.; Rasslan, S. Effect of low-dose gaseous ozone on pathogenic bacteria. *BMC Infect. Dis.* **2012**, *12*, 358. [CrossRef]
52. US EPA—Office of Water EPA Alternative Disinfection and Oxidant Guidance Manual. 1999; pp. 1–328. Available online: <https://nepis.epa.gov/Exe/ZyPDF.cgi/2000229L.PDF?Dockey=2000229L.PDF> (accessed on 6 December 2020).
53. Sharma, M.; Hudson, J.B. Ozone gas is an effective and practical antibacterial agent. *Am. J. Infect. Control* **2008**, *36*, 559–563. [CrossRef] [PubMed]
54. Kowalski, W.J.; Bahnfleth, W.P.; Whittam, T.S. Bactericidal Effects of High Airborne Ozone Concentrations on Escherichia coli and Staphylococcus aureus. *Ozone Sci. Eng.* **1998**, *20*, 205–221. [CrossRef]
55. Ouf, S.A.; Moussa, T.A.; Abd-Elmegeed, A.M.; Eltahlawy, S.R. Anti-fungal potential of ozone against some dermatophytes. *Braz. J. Microbiol.* **2016**, *47*, 697–702. [CrossRef] [PubMed]
56. Cristiano, L. Could ozone be an effective disinfection measure against the novel coronavirus (SARS-CoV-2)? *J. Prev. Med. Hyg.* **2020**, *61*, E301–E303. [CrossRef]
57. Wigginton, K.R.; Kohn, T. Virus disinfection mechanisms: The role of virus composition, structure, and function. *Curr. Opin. Virol.* **2012**, *2*, 84–89. [CrossRef]
58. Gavazza, A.; Marchegiani, A.; Rossi, G.; Franzini, M.; Spaterna, A.; Mangiaterra, S.; Cerquetella, M. Ozone Therapy as a Possible Option in COVID-19 Management. *Front. Public Heal.* **2020**, *8*, 1–7. [CrossRef]
59. Victorin, K. Review of the genotoxicity of ozone. *Mutat. Res. Genet. Toxicol.* **1992**, *277*, 221–238. [CrossRef]
60. Murray, B.K.; Ohmine, S.; Tomer, D.P.; Jensen, K.J.; Johnson, F.B.; Kirsi, J.J.; Robison, R.A.; O'Neill, K.L. Virion disruption by ozone-mediated reactive oxygen species. *J. Virol. Methods* **2008**, *153*, 74–77. [CrossRef] [PubMed]
61. Hudson, J.B.; Sharma, M.; Vimalanathan, S. Development of a Practical Method for Using Ozone Gas as a Virus Decontaminating Agent. *Ozone Sci. Eng.* **2009**, *31*, 216–223. [CrossRef]
62. Muzhi, Z. Ozone: A Powerful Weapon to Combat COVID-19 Outbreak. Available online: [http://www.china.org.cn/opinion/2020-02/26/content\\_75747237\\_4.htm](http://www.china.org.cn/opinion/2020-02/26/content_75747237_4.htm) (accessed on 13 November 2020).
63. Petry, G.; Rossato, L.G.; Nespolo, J.; Kreutz, L.C.; Bertol, C.D. In Vitro Inactivation of Herpes Virus by Ozone. *Ozone Sci. Eng.* **2014**, *36*, 249–252. [CrossRef]
64. Brié, A.; Boudaud, N.; Mssihid, A.; Loutreul, J.; Bertrand, I.; Gantzer, C. Inactivation of murine norovirus and hepatitis A virus on fresh raspberries by gaseous ozone treatment. *Food Microbiol.* **2018**, *70*, 1–6. [CrossRef] [PubMed]
65. Jiang, H.J.; Chen, N.; Shen, Z.Q.; Yin, J.; Qiu, Z.G.; Miao, J.; Yang, Z.W.; Shi, D.Y.; Wang, H.R.; Wang, X.W.; et al. Inactivation of Poliovirus by Ozone and the Impact of Ozone on the Viral Genome. *Biomed. Environ. Sci.* **2019**, *32*, 324–333. [CrossRef]
66. Białoszewski, D.; Bocian, E.; Bukowska, B.; Czajkowska, M.; Sokół-Leszczynska, B.; Tyski, S. Antimicrobial activity of ozonated water. *Med. Sci. Monit.* **2010**, *16*, MT71–MT75.
67. Bezirtzoglou, E.; Cretoi, S.-M.; Moldoveanu, M.; Alexopoulos, A.; Lazar, V.; Nakou, M. A quantitative approach to the effectiveness of ozone against microbiota organisms colonizing toothbrushes. *J. Dent.* **2008**, *36*, 600–605. [CrossRef]
68. Hubbezoglu, I.; Zan, R.; Tunc, T.; Sumer, Z.; Hurmuzlu, F. Antifungal Efficacy of Aqueous and Gaseous Ozone in Root Canals Infected by Candida albicans. *Jundishapur J. Microbiol.* **2013**, *6*, 1–3. [CrossRef]
69. World Intellectual Property Organization Frequently Asked Questions: Patents. Available online: [https://www.wipo.int/patents/en/faq\\_patents.html#:~:text=Exclusiverights%3APatentsprovideyou,filingofthepatentapplication](https://www.wipo.int/patents/en/faq_patents.html#:~:text=Exclusiverights%3APatentsprovideyou,filingofthepatentapplication) (accessed on 6 December 2020).
70. INAPI—National Institute of Industrial Property of Chile Patents: Types of Patents. Available online: <https://www.ipaustralia.gov.au/patents/understanding-patents/types-patents> (accessed on 6 December 2020).
71. Song, C.H.; Han, J.-W. Patent cliff and strategic switch: Exploring strategic design possibilities in the pharmaceutical industry. *Springerplus* **2016**, *5*, 692. [CrossRef]
72. TSO<sub>3</sub> Inc. Available online: <https://www.tso3.com/> (accessed on 19 November 2020).
73. ETHICON Inc. Available online: <https://www.jnjmedicaldevices.com/> (accessed on 19 November 2020).
74. RENOSEM CO LTD. Available online: <http://renosem.com/company/ceo-message/> (accessed on 19 November 2020).
75. World Intellectual Property Organization PCT FAQs. Available online: [https://www.wipo.int/export/sites/www/pct/en/basic\\_facts/faqs\\_about\\_the\\_pct.pdf](https://www.wipo.int/export/sites/www/pct/en/basic_facts/faqs_about_the_pct.pdf) (accessed on 5 December 2020).
76. World Intellectual Property Organization. *Patent Cooperation Treaty (PCT)*; World Intellectual Property Organization: Washington, DC, USA, 2001.
77. Schwartz, P.; Garvey, S.; Carmichael, J.; Meier, E.; Guzman-Cottrill, J. *Disinfecting Articles with Ozone*; Éclair Medical Systems Inc.: Portland, OR, USA, 2020.
78. Joshi, A. *Devices for Disinfection, Deodorization, and/or Sterilization of Objects*; Microlin LLC: Salt Lake City, UT, USA, 2019.
79. Hu, P.K.; Young, L. Ozone Sterilization. Device. Patent KR201646115A, 25 October 2017.



80. Kaisha, U.D.K. Sterile Environment Maintenance Method of Operation Chamber, Sterile Environment Maintenance. Device. Patent CN202010309498A, 13 November 2020.
81. Dufresne, S.; Martel, C.; Leblond, H.; Dassie, N.; Martel, K. *Method for Sterilizing an Article in a Sealable Sterilization Chamber*; TSO<sub>3</sub> Inc.: Québec, QC, Canada, 2018.
82. Genial Medical Gennail YC400 Walk through Disinfection Tunnel Anti COVID-19. Available online: <https://www.genialmedical.com/wz.aspx?id=44> (accessed on 21 December 2020).
83. BROAD Group Ltd. BROAD Disinfection Cabin. Available online: <http://en.broad.com/ProductShow-100.aspx> (accessed on 21 December 2020).
84. myOzone Tunnel Disinfecting People with Ozone Mist. Available online: <https://myozone.com.br/tunel-desinfetante-de-pessoas-com-nevoa-de-ozonio/> (accessed on 21 December 2020).
85. Federal Technological University of Paraná Researchers Create Disinfection Tunnel with 100% National Technology. Available online: <http://portal.utfpr.edu.br/noticias/geral/covid-19/pesquisadores-da-utfpr-desenvolvem-tunel-de-desinfeccao-com-tecnologia-100-nacional> (accessed on 21 December 2020).
86. Tropical Clean Individual Disinfection System Covid-19. Available online: <https://tropicalestufas.com.br/tropical-clean-sistema-de-desinfeccao-individual/#> (accessed on 21 December 2020).
87. Eurobras Ozonated Disinfection Chamber. Available online: <https://www.eurobras.com.br/camara-de-desinfeccao-ozonizada/> (accessed on 21 December 2020).
88. B3Zonio Ozone-Based Individual Disinfection Cabin. Available online: <https://www.b3zonio.com/cabinededesinfeccao> (accessed on 21 December 2020).
89. OZ-AIR® Ozone Based Sterilization Tunnel. Available online: <https://pdf.indiamart.com/impdf/22288383630/MY-197008/ozone-based-sterilization-tunnels.pdf> (accessed on 21 December 2020).
90. SafeWay Disinfection Cabin. Available online: <https://getsafeway.com/cabin-en> (accessed on 21 December 2020).
91. Kim, D.; Kang, D. UVC LED Irradiation Effectively Inactivates Aerosolized Viruses, Bacteria, and Fungi in a Chamber-Type Air Disinfection System. *Appl. Environ. Microbiol.* **2018**, *84*, 1–11. [CrossRef] [PubMed]
92. Hao, L.; Wu, J.; Zhang, E.; Yi, Y.; Zhang, Z.; Zhang, J.; Qi, J. Disinfection efficiency of positive pressure respiratory protective hood using fumigation sterilization cabinet. *Biosaf. Health* **2019**, *1*, 46–53. [CrossRef] [PubMed]
93. International Commission on Non-Ionizing Radiation Protection UVC LAMPS and SARS-COV-2. Available online: <https://www.icnirp.org/en/activities/news/news-article/sars-cov-2-and-uvc-lamps.html> (accessed on 21 December 2020).