

# Global trends and hot topics in clinical applications of perovskite materials: a bibliometric analysis

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## Key Words:

bibliometrics; bibliometrix; CiteSpace; perovskite; R package

## ABSTRACT

In recent years, perovskite has received increasing attention in the medical field. However, there has been a lack of related bibliometric analysis in this research field. This study aims to analyse the research status and hot topics of perovskite in the medical field from a bibliometric perspective and explore the research direction of perovskite. This study collected 1852 records of perovskite research in the medical field from 1983 to 2022 in the Web of Science (WOS) database. The country, institution, journal, cited references, and keywords were analysed using CiteSpace, VOS viewer, and Bibliometrix software. The number of articles related to perovskite research in the medical field has been increasing every year. China and USA have published the most papers and are the main forces in this research field. The University of London Imperial College of Science, Technology, and Medicine is the most active institution and has contributed the most publications. ACS Applied Materials & Interfaces is the most prolific journal in this field. "Medical electronic devices", "X-rays", and "piezoelectric materials" are the most researched directions of perovskite in the medical field. "Performance", "perovskite", and "solar cells" are the most frequently used keywords in this field. Advanced Materials is the most relevant and academically influential journal for perovskite research. Halide perovskites have been a hot topic in this field in recent years and will be a future research trend. X-ray, electronic medical equipment, and medical stents are the main research directions.

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## Introduction

Perovskite is a class of ceramic oxides named after their crystal structure, which is an octahedral cube with the general formula  $ABX_3$ . The A-site is usually composed of organic or inorganic cations (such as methylammonium, formamidinium, or inorganic cations  $Cs^+$  or  $Rb^+$ ); the B-site is composed of inorganic cations ( $Pb^{2+}$  or  $Sn^{2+}$ ); and the X-site is composed of oxygen or halides (I, Br, or Cl). The surface adsorption of oxygen and lattice oxygen on perovskite affects its catalytic activity. At lower temperatures, surface adsorbed oxygen plays a major role in oxidation; at higher temperatures, lattice oxygen plays a role.

Changing the metal elements at the A and B sites can regulate the number and activity of lattice oxygen. Substituting some of the +3-valent A and B atoms with +2 or +4-valent atoms can also generate lattice defects or lattice oxygen, thereby improving catalytic activity. This makes perovskites have excellent prospects in high-temperature catalysis and photocatalysis.<sup>1</sup>

In recent years, perovskites have been widely used in medical imaging. Medical X-ray imaging requires a reduction in diagnostic medical radiation to minimise its impact on patient health.<sup>2, 3</sup> Studies have shown that organic-metal perovskites prepared as thin films at low

temperatures and used in digital X-ray detectors have not only the advantages of low cost and large radiation area, but also low radiation dose.<sup>4</sup> Metal halide perovskites are a new type of optoelectronic material that can be used as a solution-deposited absorption layer in solar cells.<sup>5</sup> It also has the function of enhancing the water stability of halide perovskites and can be used for upconversion imaging in living cells.<sup>6</sup> Therefore, it has been widely used in the field of biological imaging. Due to the good biocompatibility and piezoelectric properties of perovskites, they are increasingly being manufactured as scaffolds for patients with fractures.<sup>7</sup> In addition, some materials can be simply encapsulated in a phospholipid protective layer through a thin film hydration method, which makes them have long-term waterproof characteristics and multi-functional biological imaging capabilities, and can be used for multi-cell imaging and *in vitro* tumour targeting.<sup>8</sup> Apart from high-temperature catalysis and photocatalysis, perovskite particles can also be used as catalysts for cellular metabolism.

Bibliometrics is the analysis of published information (such as books, journal articles, datasets, blogs) and their related metadata (such as abstracts, keywords, citations), using statistical data to describe or display relationships between published works. In recent years, bibliometric analysis has been used to analyse data, draw graphs, and show future research trends.<sup>9</sup> However, to date, no bibliometric analysis of the application of perovskites in the medical field has been found. Therefore, this study aims to analyse the research direction of perovskites in the medical field through bibliometric analysis, to understand related emerging frontier topics, and to provide direction for subsequent research.

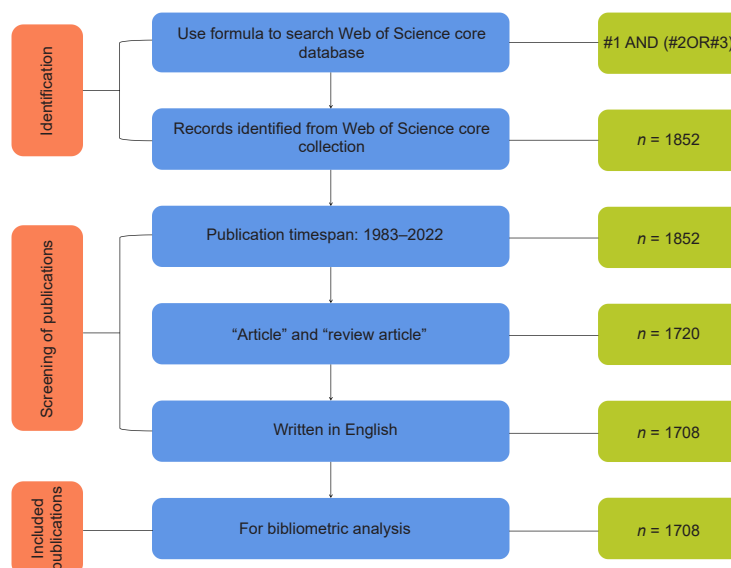
## Methods

### Documents collection and retrieval strategy

We used the Web of Science (WOS) core collection database to search relevant publications on applications of perovskite in the medical field. The WOS database includes journals, books, patents, conference proceedings, and web resources. We chose the WOS database because it provides many articles with complete information.

The search formula used was: #1AND(#2OR#3)=[((ALL=(medical)) OR ALL=(medicine)) OR ALL=(biomedical)AND(((TS=(perovskite)) OR TI=(perovskite)) OR AB=(perovskite) OR((TS=(CaTiO<sub>3</sub>)) OR TI=(CaTiO<sub>3</sub>)) OR AB=(CaTiO<sub>3</sub>)))]

Through the above search formula, a cross-sectional search was performed on December 17, 2022, and 1852 publications were retrieved from WOS in total. Finally, we reviewed and evaluated all available publication data to identify those that focused on “applications of perovskite in the medical field”. **Figure 1** illustrates the search and exclusion protocols employed in this study for identifying suitable publications from the WOS database. The literature search was limited to English publications published between 1983 and 2022. In this study, our database only included research articles and reviews. The final screening results were exported to a dataset, including citation information (author, publication title, year of publication, source title, volume, issue, page numbers, citation count, source, and publication type) and bibliographic information (affiliation, editor, keywords, and funding details). The complete records of the retrieved articles were saved and downloaded from the WOS database and saved in BibTeX format for further analysis.



**Figure 1.** Flowchart for the selection of literature included in this study.

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### Analysis tools

To describe the characteristics of all literature related to “application of perovskite in the medical field”, we used Bibliometrix (R Studio, V1.4, Posit Software, Boston, MA, USA)<sup>10</sup> and CiteSpace V5.8 R3 (Drexel University, Philadelphia, PA, USA)<sup>11</sup> to further analyse all eligible data.

### Bibliometric analysis

The dataset was imported into Bibliometrix, which can analyse annual publishing trends and create line charts. In addition, it was also used to analyse the annual publishing trends of different countries and regions, as well as different journals. The bibliometrix package was employed to produce a word cloud and thematic map illustrating the top 100 high-frequency keywords. Thematic map starts with a co-occurring keyword network and draws a typified theme for a field in a two-dimensional map. The utilization of keyword+ (KWP) enables a more accessible interpretation of the research themes established within the framework. This analysis is conducted

based on word or phrase occurrences that frequently appear in the reference titles cited within articles, but do not appear in the article titles themselves.

## Results

### General data

After searching the query, a total of 1852 articles were obtained. After undergoing additional screening, a total of 1708 articles met the inclusion criteria for the assessment system. **Table 1** presents the general information of all the included literature. The cumulative citation count for all the articles was 67,654, with an average citation frequency of 39.61 times per article. Among the included articles, there were 1584 research articles, comprising 92.7% of all publications, and 124 reviews, comprising 7.3% of all publications. Overall, 78 countries/regions, 1896 institutions, 7193 authors, and 447 journals have contributed to this field. The study also found that the number of articles published in journals increased between 2013 and 2022.

**Table 1. General information of all publications on perovskite materials in the Web of Science database**

Description	Results
<b>Main information about data</b>	
Timespan	1983–2022
Sources	447
Documents	1708
Annual growth rate (%)	4.11
Document average age (year)	5.66
Average citations per document	39.61
References	61233
<b>Document contents</b>	
Keywords plus (ID)	3480
Author's keywords (DE)	3714
<b>Authors</b>	
Total number of authors	7193
Authors of single-authored documents	15
<b>Authors collaboration</b>	
Single-authored documents	17
Co-authors per document	6.87
International co-authorships (%)	37.82
<b>Document types</b>	
Research article	1584
Review	124

Note: DE: the field identifier of the Author's Keywords; ID: the field identifier Of 'Keywords Plus' in the Web Of Science.

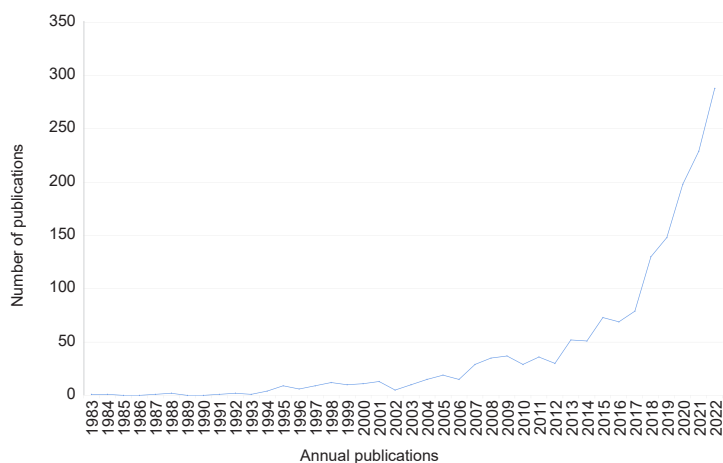
### Publication trend

The number of newly published papers in the field of perovskite medical applications is depicted in **Figure 2**. The overall trajectory exhibits an upward trend, with a growth rate of 15.21%, dividing into two distinct periods. The first period spans from 1983 to 2012, during which the annual number of new publications in this field remained below 50. This period demonstrates a relatively stable trend, with an average annual growth rate of 8.38%. The second period covers the years 2013 to 2022, witnessing an annual increase of more than 50 publications, indicating a notable overall upward trend with

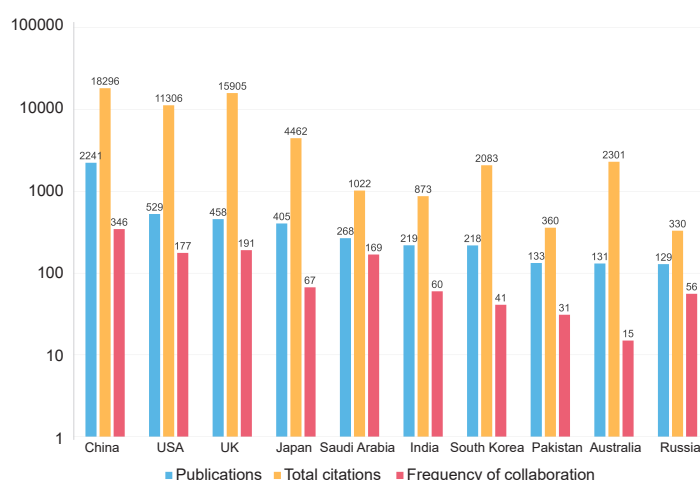
an annual growth rate of 18.3%. It is worth noting that the number of new publications added in 2014 and 2016 is slightly lower than the previous year.

### Country/region

**Figure 3** presents a ranking of the top ten countries/regions that have made significant contributions in this field. China takes the lead with 2241 published papers, followed by USA with 529 papers, and UK with 458 papers. The region with the highest number of publications is Asia, accounting for 46.76% of all publications, followed by Europe, accounting for



**Figure 2.** Number of publications related to novel clinical applications of perovskite materials in the Web of Science database (1983–2022).



**Figure 3.** Top ten most productive countries/regions of all publications on perovskite materials in the Web of Science database.

30.23% of all publications. China is the most prolific country in Asia, and UK is the most prolific country in Europe. In terms of citations, China has the highest total number of citations (TC) ( $n = 18,296$ ) and frequency of collaboration ( $n = 348$ ); UK ranks second in TC ( $n = 15,905$ ) and frequency of collaboration ( $n = 191$ ); USA ranks third in TC ( $n = 11,306$ ) and frequency of collaboration ( $n = 177$ ).

### Institution

**Figure 4A** shows the top ten institutions with the highest output in the field of perovskite medical applications based on the number of publications. The institution with the most publications is the University of London Imperial College of Science, Technology, and Medicine (210 publications), followed by the Chinese Academy of Sciences (91 publications) and King Saud University (59 publications). In terms of total citations, the University of London Imperial College of Science, Technology, and Medicine is again the top institution (with 18,834 citations), followed by the Chinese Academy of Sciences (3457 citations) and Southeast University (2334

citations). Among all institutions, London Imperial College of Science, Technology, and Medicine (with 90 citations per article) has the highest average citation frequency per article, followed by the National University of Singapore (72 citations per article) and the University of Cambridge (72 citations per article). Among the top ten most prolific institutions, five are in China, two are in the UK, and the other three are in Japan, Singapore, and Saudi Arabia.

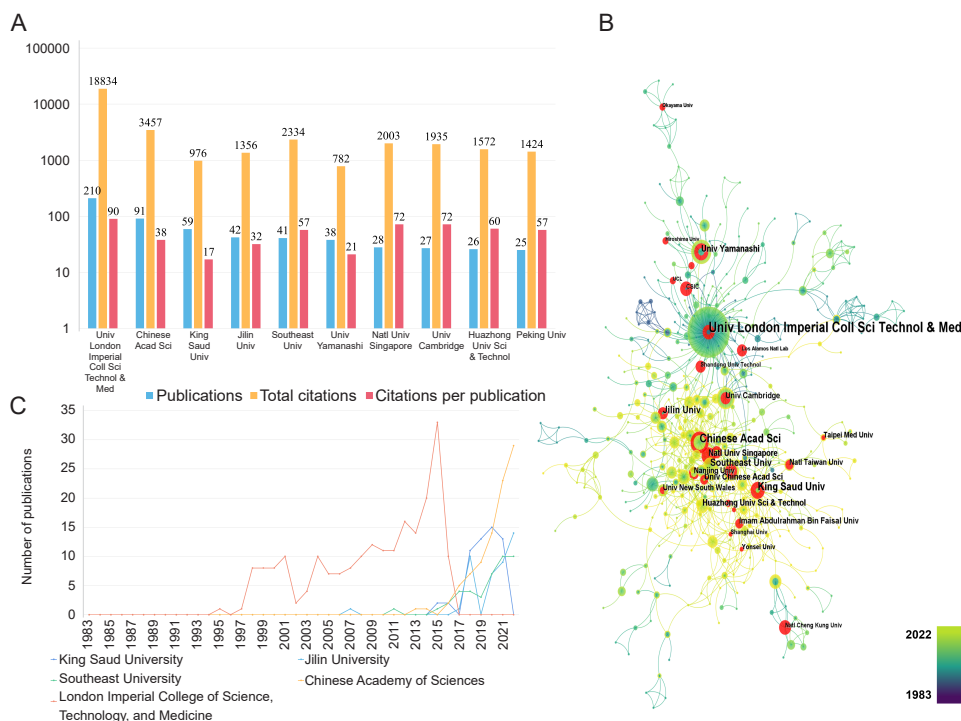
In **Figure 4B**, a co-authorship network map of institutions is shown. The map reveals clusters of closely collaborating institutions. The largest cluster includes the Chinese Academy of Sciences, King Saud University, and the National University of Singapore, indicating that these institutions have close collaborative relationships, with the most participating institutions from China. Notable examples include the Imperial College of Science, Technology, and Medicine at the University of London and the Chinese Academy of Sciences.

**Figure 4C** shows a line chart that reflects the number of publications per year for the five most prolific institutions. The

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University of London Imperial College of Science, Technology, and Medicine has been publishing articles in this field since 1997 and has the highest number of publications, citations, and average citations per article. The other four institutions started

publishing more articles after 2015, with the Chinese Academy of Sciences showing a significant increase in publications since 2013. Southeast University has fewer publications than the Chinese Academy of Sciences, but it is also trending upward overall.



**Figure 4.** Keyword co-occurrence analysis of all publications on perovskite materials in the Web of Science database. (A) The number of articles published, the number of articles applied, and the average number of articles applied in VOS viewer. (B) Use VOS viewer to visualize the institutional co-occurrence network. Large nodes indicate that the occurrence rate of keywords is higher. The same colour indicates a close relationship. (C) Annual number of publications by the top five most productive institutions. In each group, the larger the node, the higher the frequency of the keyword; the denser the line, the closer their relationship. “Conversion” and “highly performance” not only have a high frequency of appearance, but also have a close relationship.

## Journal

**Table 2** shows the top nine most prolific journals and most cited journals in the field of perovskite materials. *ACS Applied Materials & Interfaces* (impact factor (2021) 10.38, Q1) is the most prolific journal with 46 publications (16.25% of the total), followed by *Solid State Ionics* (impact factor (2021) 3.70, Q2) with 40 publications, and *Chinese Chemical Letters* (impact factor (2021) 8.46, Q1) with 39 publications. In terms of citation and impact, *Solid State Ionics* ranks first (4396 TC, H-index 25), followed by *Advanced Materials* (2440 TC, H-index 21) and *ACS Applied Materials & Interfaces* (1051 TC, H-index 18). It's worth noting that the number of publications alone may not accurately reflect a country's or institution's influence in a given field. Therefore, we employed VOS viewer to identify the most frequently cited journals in the field of perovskite materials. The top three most cited journals are *Advanced Materials* (777 citations), *Journal of the American Chemical Society* (740 citations), and *Science* (736 citations).

## Top cited articles

To ascertain the most influential research in this field, we utilized bibliometrics to extract the top ten most cited papers with the highest number of citations. The ten most cited papers are listed in **Table 3**. The most cited paper (73 local citations) was published by Yong Churl Kim in *Nature* in 2017, titled “Printable organometallic perovskite enables large-area, low-dose X-ray imaging”. In this paper, the author discovered that perovskite films can control dark currents and instantaneous charge carrier transport, enabling low-dose X-ray imaging, as well as being used for radiation imaging, sensing, and energy harvesting photodetectors. In addition, four papers<sup>12–15</sup> reported on the relevant information of lead halide perovskites. Only one review introduces the past and present development of halide perovskite, as well as its prospects for the future.<sup>12</sup> The other three articles respectively introduce the relevant knowledge of halide perovskite with X-ray<sup>13, 14</sup> and gamma photons.<sup>15</sup>

**Table 2. The top nine most prolific journals and co-cited journals with the most publications related to novel clinical applications of perovskite materials**

Rank	Journal	Publications <sup>a</sup>	Total citations	H index	Impact factor (2021)	Co-cited journal	Co-citations	Impact factor (2021) of co-cited journal
1	<i>Solid State Ionics</i>	40	4396	25	3.7	<i>Advanced Materials</i>	777	32.09
2	<i>Advanced Materials</i>	29	2440	21	32.09	<i>Journal of the American Chemical Society</i>	740	16.38
3	<i>ACS Applied Materials &amp; Interfaces</i>	46	1051	18	10.38	<i>Science</i>	736	63.71
4	<i>Journal of Materials Chemistry A</i>	24	1073	18	19.92	<i>Nature</i>	717	69.5
5	<i>Advanced Functional Materials</i>	30	1118	15	3.75	<i>Chemistry of Materials</i>	607	10.51
6	<i>Chemistry of Materials</i>	23	2263	15	10.51	<i>Nature Communications</i>	601	17.69
7	<i>Chinese Chemical Letters</i>	39	715	15	8.46	<i>ACS Applied Materials &amp; Interfaces</i>	582	10.38
8	<i>Journal of Materials Chemistry C</i>	28	473	13	8.07	<i>Advanced Functional Materials</i>	574	19.92
9	<i>Journal of Alloys and Compounds</i>	24	595	12	6.37	<i>Nano Letters</i>	535	12.26

Note: <sup>a</sup>The publication refers to an article that has been published in a journal and expresses information and knowledge in a certain way, including text, images, and tables

**Table 3. The top ten most cited publications with the most publications related to novel clinical applications of perovskite materials**

Rank	First Author	Title	Local citations	Journal	Publication year
1	Yong Churl Kim	<i>Printable organometallic perovskite enables large-area, low-dose X-ray imaging</i>	73	<i>Nature</i>	2017
2	Qiushui Chen	<i>All-inorganic perovskite nanocrystal scintillators</i>	70	<i>Nature</i>	2018
3	Weicheng Pan	<i>Cs<sub>2</sub>AgBiBr<sub>6</sub> single-crystal X-ray detectors with a low detection limit</i>	60	<i>Nature</i>	2017
4	Renzhong Zhuang	<i>Highly sensitive X-ray detector made of layered perovskite-like (NH<sub>4</sub>)<sub>3</sub>Bi<sub>2</sub>I<sub>9</sub> single crystal with anisotropic response</i>	35	<i>Nature</i>	2019
5	Ajay Kumar Jena	<i>Halide perovskite photovoltaics: background, status, and future prospects</i>	31	<i>Chemical Reviews</i>	2019
6	Yuhai Zhang	<i>Metal halide perovskite nanosheet for X-ray high-resolution scintillation imaging screens</i>	29	<i>ACS Nano</i>	2019
7	Yunxia Zhang	<i>Nucleation-controlled growth of superior lead-free perovskite Cs<sub>3</sub>Bi<sub>2</sub>I<sub>9</sub> single-crystals for high-performance X-ray detection</i>	29	<i>Nature Communications</i>	2020
8	Sergii Yakunin	<i>Detection of gamma photons using solution-grown single crystals of hybrid lead halide perovskites</i>	27	<i>Nature</i>	2016
9	M D Birowosuto	<i>X-ray scintillation in lead halide perovskite crystals</i>	24	<i>Scientific Reports</i>	2016
10	Weicheng Pan	<i>Hot-pressed CsPbBr<sub>3</sub> quasi-monocrystalline film for sensitive direct X-ray detection</i>	23	<i>Advanced Materials</i>	2019

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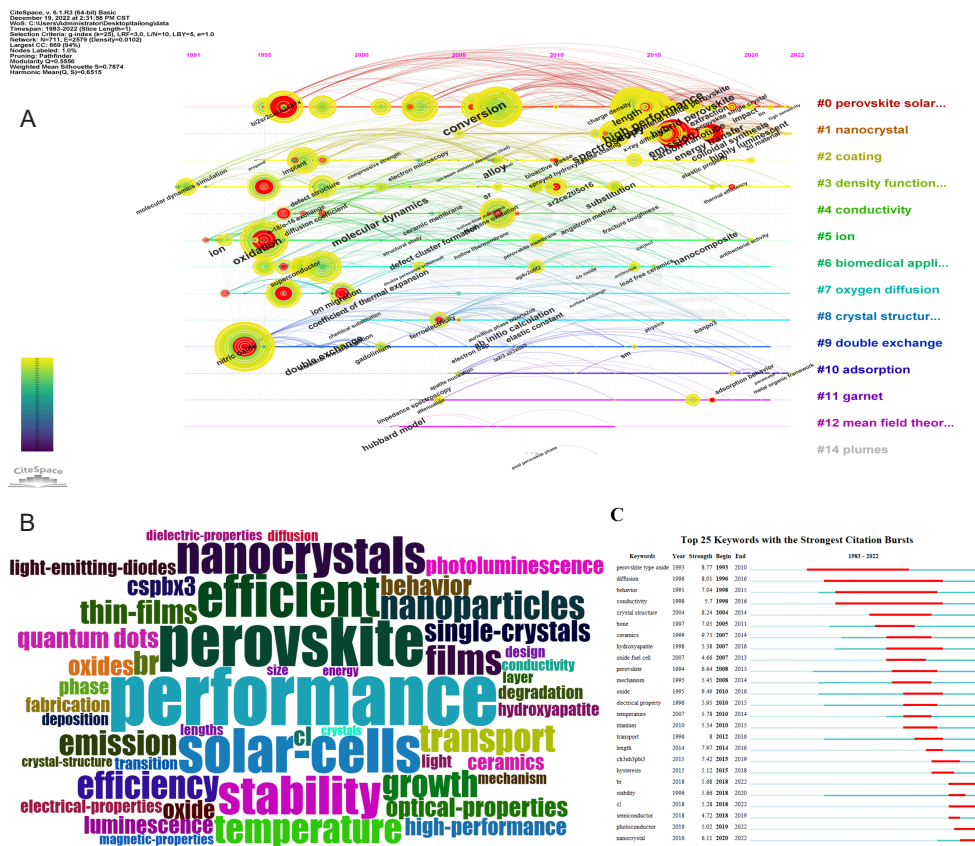
## Keywords' evolution

Keyword analysis is used to summarise and convey the thesis topic. **Figure 5A** shows co-occurring keyword analysis, grouping similar keywords together using "site space". The study merges 50 keywords into 14 groups, such as energy transfer, colloidal synthesis, and highly luminescent, which can be grouped under nanocrystal. The research hotspots are "oxidation," "hybrid perovskite", and "carbon nanotube".

**Figure 5B** lists the most commonly used keywords, with larger font sizes indicating higher citation frequencies. The top ten most frequently used keywords are "performance" ( $n = 168$ ),

"perovskite" ( $n = 141$ ), "solar-cells" ( $n = 127$ ), "efficient" ( $n = 122$ ), "stability" ( $n = 111$ ), "nanocrystals" ( $n = 107$ ), "films" ( $n = 85$ ), "temperature" ( $n = 84$ ), "nanoparticles" ( $n = 82$ ), and "transport" ( $n = 81$ ).

**Figure 5C** illustrates the top 25 keywords exhibiting notable citation bursts in the field of perovskites. The active and non-active periods are represented by red and blue, respectively. Starting from 2010, keywords such as "nanocrystal", "Br", "Cl", "photoconductor" and "semiconductor" have been consistently utilized.



**Figure 5.** Keyword co-occurrence analysis of all publications on perovskite materials in the Web of Science database. (A) Use VOS viewer to visualize author keyword co-occurrence network. (B) Keywords that appear the most. The larger the font, the higher the frequency of keywords. (C) The initial keyword with the most significant citation burst signifies the prominent topics during different time periods. The red bars indicate the duration of the burst period, highlighting the intensification of interest. The strength of the burst indicates the importance of the topic to the field of study.

## Discussion

Over the past few decades, researchers have conducted extensive studies on the application of perovskites in the medical field. A comprehensive analysis of research related to perovskites was conducted using bibliometric analysis, exploring publications, countries, institutions, journals, most cited articles, and keywords.

## Global publication trends and countries/regions

The increasing number of publications in the field of perovskite medical applications indicates a growing interest and research

focus in this area. The steady increase in the number of newly published papers since 2013 suggests that researchers are recognising the potential of perovskite materials in medical applications. The involvement of multiple countries, institutions, authors, and journals highlights the collaborative nature of research in this field. Collaboration between different entities can lead to the exchange of ideas, expertise, and resources, contributing to scientific advancements. China emerges as the leading contributor in terms of the number of published papers. This demonstrates China's active involvement and significant research output in perovskite

medical applications. It also reflects China's commitment to scientific research and development. Among them, the high efficiency and low cost of perovskite solar cells made in China have attracted worldwide attention.<sup>16</sup>

Asia and Europe are the leading regions in terms of publication output. This suggests that researchers from these regions are at the forefront of exploring the applications of perovskite materials in medicine. The high number of publications from these regions signifies their expertise and contributions to the field. The cumulative citation count and average citation frequency indicate the impact and visibility of the published articles. A higher number of citations suggests that the research conducted in this field has gained attention and recognition within the scientific community. Overall, the analysis underscores the growing research interest in perovskite medical applications, the collaborative nature of scientific exploration, and the significant contributions of China, Asia, and Europe in advancing this field. These findings provide a foundation for further research and development in leveraging perovskite materials for medical applications.

### Institutions

The influence and contribution of research institutions represent the research level of a country or region. Among the top ten most prolific institutions, five are in China and two are located in UK. The University of London Imperial College of Science, Technology and Medicine in UK is the most productive institution, publishing the most papers on the application of perovskites in the medical field, and each paper is cited on average the most times. This research institution focuses on the problems and solutions encountered in the application of halide perovskites. Their recent research shows that tin halide perovskites are the preferred option for lead-free perovskite optoelectronic devices.<sup>17</sup> In China, the institution with the most papers and citations is the Chinese Academy of Sciences, which has focused on perovskite solar cells in recent years.

### Journals and co-citation journals

In terms of publication output, *ACS Applied Materials & Interfaces* is the most prolific journal with 46 publications, representing 16.25% of the total. It is followed by *Solid State Ionics* with 40 publications and *Chinese Chemical Letters* with 39 publications. These journals have a significant contribution to the dissemination of research in the field. However, when considering citation impact, *Solid State Ionics* ranks first with 4396 total citations and a 25-H-index. This indicates that the articles published in *Solid State Ionics* have generated a substantial impact and have been widely cited.

Furthermore, it is important to note that the number of publications alone may not accurately reflect the influence of a country or institution in a specific field. Therefore, additional analysis was conducted using VOS viewer to identify frequently cited journals in the field of perovskite materials. The results reveal that *Advanced Materials* is the most frequently cited journal, with 777 citations. It is followed by *Journal of the American Chemical Society* with 740 citations and *Science* with 736 citations. These highly cited journals

indicate their significance and impact in the field of perovskite materials research.

In conclusion, while *ACS Applied Materials & Interfaces*, *Solid State Ionics*, and *Chinese Chemical Letters* are the top prolific journals in terms of publication output, *Advanced Materials*, *Journal of the American Chemical Society*, and *Science* are the most frequently cited journals, highlighting their influence and importance in the field. Researchers should consider publishing their work in these high-impact journals to maximise visibility and potential citations.

### Most cited references

Among all publications, the article most frequently cited is "Printable organometallic perovskite enables large-area, low-dose X-ray imaging" by Kim et al.<sup>4</sup> The authors found that solution-processed perovskite detectors can achieve low-dose X-ray imaging and can also be used for radiation imaging, sensing, and energy harvesting in optoelectronic devices. This article provides theoretical support for the widespread application of perovskites in X-ray medical imaging in the future. The most cited review is "Halide perovskite photovoltaics: background, status, and future prospects" by Jena et al.,<sup>12</sup> which is a comprehensive review of past research, current status, and future prospects of halide perovskites. The article focuses on summarizing the principles and latest advances in X-ray detectors and solar cells, laying the foundation for future related research.

### Research hotspots and frontier trends

In the past, research on perovskite materials was mainly focused on inorganic oxides, such as ceramics, hydroxyapatite, and perovskite-type oxide. As research continues to deepen, halide and organic oxides are also receiving attention. The physical and chemical properties of perovskites, such as hysteresis, electrical properties, and conductivity, have always been a focus of research.

### Perovskites and X-rays

X-rays play a crucial role in the medical field due to their penetrating effect, differential absorption, photosensitivity, and fluorescence. They can assist doctors in diagnosing diseases more accurately.<sup>18</sup> However, X-rays are also one of the most widely used sources of radiation in medical diagnosis and treatment, and ionisation and radiation can cause protein decomposition, leading to damage to the human body. Long-term radiation exposure can cause DNA molecule breakage and increase the risk of cancer.<sup>19, 20</sup> Therefore, reducing radiation and improving imaging quality is an urgent problem that needs to be addressed. In recent years, scientists have found that materials such as  $(\text{NH}_4)_3\text{Bi}_2\text{I}_9$  single crystals,  $\text{Cs}_3\text{Bi}_2\text{I}_9$  perovskite single crystals, and colloidal perovskite nanosheets ( $\text{CsPbBr}_3$ ) have high sensitivity, low radiation, and high imaging quality.<sup>13, 21</sup> This shows that perovskites can reduce radiation and improve X-ray imaging quality, further improving their clinical applications.

### Perovskites and medical electronic devices

With the development of society, energy demand is constantly increasing, and innovative solutions for efficient energy



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harvesting are needed. In modern medical diagnostic and treatment methods, implantable biomedical electronic devices can improve patients' clinical outcomes and provide a large amount of data about the patients themselves, so they need to be small and lightweight. However, energy storage is still one of the obstacles affecting energy applications.<sup>22, 23</sup> The development of medical electronic devices aims to reduce energy consumption while also being able to extract energy from the environment, and solar cells are just the right solution. Sunlight is the easiest to obtain and cleanest source of energy. After the battery is implanted under the skin, it can obtain energy through solar radiation. However, the application of solar cells in the human body is limited by many factors. Firstly, they need to have good biocompatibility. Poon et al.'s experiment<sup>24</sup> has shown that cells grown on perovskite material surfaces have good metabolism and can be implanted in the human body for a long time while also having good piezoelectric properties. In terms of optical properties, Aminzare et al.<sup>25</sup> found that perovskites also exhibit efficient radiation recombination and coordinated spectral emission, with good photoelectric properties.

However, perovskite solar cells also have some problems, such as the incompatibility of halide ions with other ions, which can become charge traps and aggravate ion migration, severely affecting the efficiency and stability of the battery. Trap-mediated nonradiative charge recombination at the surface is one of the main limitations for achieving highly efficient metal halide perovskite photovoltaics.<sup>26, 27</sup> Zhang et al.<sup>28</sup> found that dual-functional cellulose can significantly reduce trap states, thus significantly suppressing nonradiative recombination and improving the power conversion efficiency of perovskite solar cells. Polyethylene glycol diacrylate can passivate surface defects in perovskite thin films to improve power conversion efficiency.<sup>29</sup> The defects in perovskite solar cells can be compensated for by other materials, and new materials are constantly being discovered and manufactured.

### *Perovskites and medical materials*

Bones have strong regenerative abilities, but when the body's self-healing ability is exceeded, transplantation is required. Autogenous bone transplantation and allogeneic bone transplantation are not widely applicable due to quantity limitations. Therefore, suitable scaffolds are crucial for bone fracture healing.<sup>30</sup> There are many types of materials used to make scaffolds, including metal materials, polymer materials, and inorganic materials.<sup>31</sup> Regardless of the material used, good biocompatibility, biodegradability, and mechanical strength are required.<sup>32</sup> Metal materials such as Mg and Zn can promote bone generation but have moderate mechanical properties. Polymer materials such as polylactic acid have good flexibility but are brittle. Inorganic materials such as hydroxyapatite have good biocompatibility but poor mechanical strength. These materials all have advantages and disadvantages and can be improved or combined with other materials to make scaffolds to help patients with bone fractures recover.<sup>33, 34</sup> In recent years, biocompatible piezoelectric materials have received widespread attention due to their piezoelectric properties similar to those of human bones.<sup>35</sup> Biocompatible

piezoelectric materials can come into contact and interact with human tissues in the body, produce local currents, restore damaged electrophysiological microenvironments, and promote bone regeneration.<sup>36, 37</sup> Some perovskites have piezoelectric properties, which have great potential in scaffold preparation. Bagchi et al.<sup>7</sup> found that perovskite ceramics such as calcium titanate and strontium titanate are compatible with cells, significantly enhance the expression of osteogenic genes, and promote bone regeneration. Dai et al.<sup>38</sup> found that barium titanate and polylactic acid piezoelectric composite materials can promote bone tissue regeneration and have strong osteogenic effects.

### *Perovskites and enzymes*

There are many ways to treat cancer, and inducing cell pyroptosis is one of the new treatment methods. Pyroptosis is a new type of cell death that also belongs to programmed cell death, including membrane perforation, cell swelling, and cell rupture.<sup>39</sup> Unlike apoptosis, pyroptotic cells swell and release cell contents, such as the typical inflammasome.<sup>40</sup> Chang et al.<sup>41</sup> found that perovskite nanoenzymes can induce cell pyroptosis and have significant therapeutic effects on cancer through *in vitro* cell and *in vivo* animal experiments. In addition to direct application in clinical treatment, perovskites can also be used in biochemical research. Nanoenzymes synthesised by perovskite oxide BiFeO<sub>3</sub> have peroxidase-like activity and can measure creatinine levels in human serum.<sup>42</sup>

### **Limitations**

There are several limitations to current research. First, only one database (WOS) was searched, and other databases and sources of information are not included in the bibliometric analysis of this article. Therefore, some potentially valuable information may have been missed. Second, because many authors are from China and their name abbreviations are repeated, no research was conducted in the "Results" section. Third, bibliometric analysis often uses citations to evaluate publishing quality. The application of perovskite in the medical field needs more study and more in-depth and comprehensive research.

### **Conclusion**

In conclusion, research on perovskite materials in the medical field has been on the rise over the past 40 years, with a significant increase in the number of publications in the last 20 years. China has emerged as a major contributor to this field with the largest number of publications and collaborations with other countries. There is great potential for China to further develop its research in this area in the future.

*Advanced Materials* is the most relevant and influential journal in the field of perovskite research in medicine. Halide perovskites have become a hot research topic in recent years and are expected to be a future research trend. X-rays, medical electronic devices, and medical materials are the main research directions.

### **Author contributions**

Design: WC; data collect: MXY; data analysis: TLS, MXY, YFZ, JSB; manuscript draft: TLS, CR; manuscript revision: TLS, HCW, XC, CL, WC. All authors have read and approved the final version of the manuscript.

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**Conflicts of interest statement**

All authors declare that they have no conflict of interest.

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1. Correa-Baena, J. P.; Saliba, M.; Buonassisi, T.; Grätzel, M.; Abate, A.; Tress, W.; Hagfeldt, A. Promises and challenges of perovskite solar cells. *Science*. **2017**, *358*, 739-744.
2. Sinnott, B.; Ron, E.; Schneider, A. B. Exposing the thyroid to radiation: a review of its current extent, risks, and implications. *Endocr Rev*. **2010**, *31*, 756-773.
3. Meedeniya, D.; Kumarasinghe, H.; Kolonne, S.; Fernando, C.; Díez, I. T.; Marques, G. Chest X-ray analysis empowered with deep learning: a systematic review. *Appl Soft Comput*. **2022**, *126*, 109319.
4. Kim, Y. C.; Kim, K. H.; Son, D. Y.; Jeong, D. N.; Seo, J. Y.; Choi, Y. S.; Han, I. T.; Lee, S. Y.; Park, N. G. Printable organometallic perovskite enables large-area, low-dose X-ray imaging. *Nature*. **2017**, *550*, 87-91.
5. Protesescu, L.; Yakunin, S.; Bodnarchuk, M. I.; Krieg, F.; Caputo, R.; Hendon, C. H.; Yang, R. X.; Walsh, A.; Kovalenko, M. V. Nanocrystals of cesium lead halide perovskites (CsPbX<sub>3</sub>, X = Cl, Br, and I): novel optoelectronic materials showing bright emission with wide color gamut. *Nano Lett*. **2015**, *15*, 3692-3696.
6. Talianov, P. M.; Peltek, O. O.; Masharin, M.; Khubezhov, S.; Baranov, M. A.; Drabavičius, A.; Timin, A. S.; Zelenkov, L. E.; Pushkarev, A. P.; Makarov, S. V.; Zyuzin, M. V. Halide perovskite nanocrystals with enhanced water stability for upconversion imaging in a living cell. *J Phys Chem Lett*. **2021**, *12*, 8991-8998.
7. Bagchi, A.; Meka, S. R.; Rao, B. N.; Chatterjee, K. Perovskite ceramic nanoparticles in polymer composites for augmenting bone tissue regeneration. *Nanotechnology*. **2014**, *25*, 485101.
8. Yang, Z.; Xu, J.; Zong, S.; Xu, S.; Zhu, D.; Zhang, Y.; Chen, C.; Wang, C.; Wang, Z.; Cui, Y. Lead halide perovskite nanocrystals-phospholipid micelles and their biological applications: multiplex cellular imaging and in vitro tumor targeting. *ACS Appl Mater Interfaces*. **2019**, *11*, 47671-47679.
9. Wu, K.; Liu, Y.; Liu, L.; Peng, Y.; Pang, H.; Sun, X.; Xia, D. Emerging trends and research foci in tumor microenvironment of pancreatic cancer: a bibliometric and visualized study. *Front Oncol*. **2022**, *12*, 810774.
10. Aria, M.; Cuccurullo, C. bibliometrix: An R-tool for comprehensive science mapping analysis. *J Informetr*. **2017**, *11*, 959-975.
11. Mao, M.; Zhou, Y.; Jiao, Y.; Yin, S.; Cheung, C.; Yu, W.; Gao, P.; Yang, L. Bibliometric and visual analysis of research on the links between the gut microbiota and pain from 2002 to 2021. *Front Med (Lausanne)*. **2022**, *9*, 975376.
12. Jena, A. K.; Kulkarni, A.; Miyasaka, T. Halide perovskite photovoltaics: background, status, and future prospects. *Chem Rev*. **2019**, *119*, 3036-3103.
13. Zhang, Y.; Sun, R.; Ou, X.; Fu, K.; Chen, Q.; Ding, Y.; Xu, L. J.; Liu, L.; Han, Y.; Malko, A. V.; Liu, X.; Yang, H.; Bakr, O. M.; Liu, H.; Mohammed, O. F. Metal halide perovskite nanosheet for X-ray high-resolution scintillation imaging screens. *ACS Nano*. **2019**, *13*, 2520-2525.
14. Birowosuto, M. D.; Cortecchia, D.; Drozdowski, W.; Brylew, K.; Lachmanski, W.; Bruno, A.; Soci, C. X-ray scintillation in lead halide perovskite crystals. *Sci Rep*. **2016**, *6*, 37254.
15. Yakunin, S.; Dirin, D. N.; Shynkarenko, Y.; Morad, V.; Cherniukh, I.; Nazarenko, O.; Kreil, D.; Nauser, T.; Kovalenko, M. V. Detection of gamma photons using solution-grown single crystals of hybrid lead halide perovskites. *Nat Photon*. **2016**, *10*, 585-589.
16. Cui, D.; Wang, Y.; Han, L. China's progress of perovskite solar cells in 2019. *Sci Bull (Beijing)*. **2020**, *65*, 1306-1315.
17. Lanzetta, L.; Webb, T.; Marin-Beloqui, J. M.; Macdonald, T. J.; Haque, S. A. Halide chemistry in tin perovskite optoelectronics: bottlenecks and opportunities. *Angew Chem Int Ed Engl*. **2023**, *62*, e202213966.
18. Pu, H.; Gao, P.; Rong, J.; Zhang, W.; Liu, T.; Lu, H. Spectral-resolved cone-beam X-ray luminescence computed tomography with principle component analysis. *Biomed Opt Express*. **2018**, *9*, 2844-2858.
19. Sauer, K.; Zizak, I.; Forien, J. B.; Rack, A.; Scoppola, E.; Zaslansky, P. Primary radiation damage in bone evolves via collagen destruction by photoelectrons and secondary emission self-absorption. *Nat Commun*. **2022**, *13*, 7829.
20. Shi, H. M.; Sun, Z. C.; Ju, F. H. Recommendations for reducing exposure to medical X-ray irradiation (review). *Med Int (Lond)*. **2022**, *2*, 22.
21. Zhang, Y.; Liu, Y.; Xu, Z.; Ye, H.; Yang, Z.; You, J.; Liu, M.; He, Y.; Kanatzidis, M. G.; Liu, S. F. Nucleation-controlled growth of superior lead-free perovskite Cs<sub>3</sub>(Bi<sub>2</sub>)I<sub>9</sub> single-crystals for high-performance X-ray detection. *Nat Commun*. **2020**, *11*, 2304.
22. Norton, C.; Hassan, U. Bioelectronic sensor with magnetic modulation to quantify phagocytic activity of blood cells employing machine learning. *ACS Sens*. **2022**, *7*, 1936-1945.
23. Klimpel, M.; Kovalenko, M. V.; Kravchuk, K. V. Advances and challenges of aluminum-sulfur batteries. *Commun Chem*. **2022**, *5*, 77.
24. Poon, K. K.; Wurm, M. C.; Evans, D. M.; Einarsrud, M. A.; Lutz, R.; Glaum, J. Biocompatibility of (Ba,Ca)(Zr,Ti)O<sub>3</sub> piezoelectric ceramics for bone replacement materials. *J Biomed Mater Res B Appl Biomater*. **2020**, *108*, 1295-1303.
25. Aminzare, M.; Jiang, J.; Mandl, G. A.; Mahshid, S.; Capobianco, J. A.; Dorval Courchesne, N. M. Biomolecules incorporated in halide perovskite nanocrystals: synthesis, optical properties, and applications. *Nanoscale*. **2023**, *15*, 2997-3031.
26. Wang, R.; Xue, J.; Wang, K. L.; Wang, Z. K.; Luo, Y.; Fenning, D.; Xu, G.; Nuryyeva, S.; Huang, T.; Zhao, Y.; Yang, J. L.; Zhu, J.; Wang, M.; Tan, S.; Yavuz, I.; Houk, K. N.; Yang, Y. Constructive molecular configurations for surface-defect passivation of perovskite photovoltaics. *Science*. **2019**, *366*, 1509-1513.
27. Gu, X.; Xiang, W.; Tian, Q.; Liu, S. F. Rational surface-defect control via designed passivation for high-efficiency inorganic perovskite solar cells. *Angew Chem Int Ed Engl*. **2021**, *60*, 23164-23170.
28. Zhang, Z.; Wang, C.; Li, F.; Liang, L.; Huang, L.; Chen, L.; Ni, Y.; Gao, P.; Wu, H. Bifunctional cellulose interlayer enabled efficient perovskite solar cells with simultaneously enhanced efficiency and stability. *Adv Sci (Weinh)*. **2023**, *10*, e2207202.
29. Xu, W.; Zhu, T.; Wu, H.; Liu, L.; Gong, X. Poly(ethylene glycol) diacrylate as the passivation layer for high-performance perovskite solar cells. *ACS Appl Mater Interfaces*. **2020**, *12*, 45045-45055.

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30. Sun, Y.; Jia, X.; Meng, Q. Characteristic evaluation of recombinant MiSp/poly(lactic-co-glycolic) acid (PLGA) nanofiber scaffolds as potential scaffolds for bone tissue engineering. *Int J Mol Sci.* **2023**, *24*, 1219.
31. Li, Y.; Chen, S. K.; Li, L.; Qin, L.; Wang, X. L.; Lai, Y. X. Bone defect animal models for testing efficacy of bone substitute biomaterials. *J Orthop Translat.* **2015**, *3*, 95-104.
32. Li, C.; Lv, H.; Du, Y.; Zhu, W.; Yang, W.; Wang, X.; Wang, J.; Chen, W. Biologically modified implantation as therapeutic bioabsorbable materials for bone defect repair. *Regen Ther.* **2022**, *19*, 9-23.
33. Jodati, H.; Evis, Z.; Tezcaner, A.; Alshemary, A. Z.; Motameni, A. 3D porous bioceramic based boron-doped hydroxyapatite/baghdadite composite scaffolds for bone tissue engineering. *J Mech Behav Biomed Mater.* **2023**, *140*, 105722.
34. Kulkarni, N. B.; Goyal, S. Comparison of bracket failure rate between two different materials used to fabricate transfer trays for indirect orthodontic bonding. *J Contemp Dent Pract.* **2022**, *23*, 307-312.
35. Khare, D.; Basu, B.; Dubey, A. K. Electrical stimulation and piezoelectric biomaterials for bone tissue engineering applications. *Biomaterials.* **2020**, *258*, 120280.
36. Xu, Q.; Gao, X.; Zhao, S.; Liu, Y. N.; Zhang, D.; Zhou, K.; Khanbareh, H.; Chen, W.; Zhang, Y.; Bowen, C. Construction of bio-piezoelectric platforms: from structures and synthesis to applications. *Adv Mater.* **2021**, *33*, e2008452.
37. Mokhtari, F.; Azimi, B.; Salehi, M.; Hashemikia, S.; Danti, S. Recent advances of polymer-based piezoelectric composites for biomedical applications. *J Mech Behav Biomed Mater.* **2021**, *122*, 104669.
38. Dai, X.; Yao, X.; Zhang, W.; Cui, H.; Ren, Y.; Deng, J.; Zhang, X. The osteogenic role of barium titanate/poly(lactic acid) piezoelectric composite membranes as guiding membranes for bone tissue regeneration. *Int J Nanomedicine.* **2022**, *17*, 4339-4353.
39. Wang, S.; Liao, X.; Xiong, X.; Feng, D.; Zhu, W.; Zheng, B.; Li, Y.; Yang, L.; Wei, Q. Pyroptosis in urinary malignancies: a literature review. *Discov Oncol.* **2023**, *14*, 12.
40. Li, L.; Wang, S.; Zhou, W. Balance cell apoptosis and pyroptosis of caspase-3-activating chemotherapy for better antitumor therapy. *Cancers (Basel).* **2022**, *15*, 26.
41. Chang, M.; Wang, Z.; Dong, C.; Zhou, R.; Chen, L.; Huang, H.; Feng, W.; Wang, Z.; Wang, Y.; Chen, Y. Ultrasound-amplified enzymodynamic tumor therapy by perovskite nanoenzyme-enabled cell pyroptosis and cascade catalysis. *Adv Mater.* **2023**, *35*, e2208817.
42. Zhu, J.; Pan, J.; Li, Y.; Yang, J.; Ye, B. Enzyme-nanozyme cascade colorimetric sensor platform: a sensitive method for detecting human serum creatinine. *Anal Bioanal Chem.* **2022**, *414*, 6271-6280.

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