



## 4D printing applications in medical field: A brief review

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### ARTICLE INFO

#### Keywords:

3D printing  
4D printing  
Customisation  
Implant  
Medical applications  
Smart material

### ABSTRACT

**Background/objectives:** There are promising applications of 4D printing in the medical field. The need is to identify the research status and explore where this new set of technologies effectively can be deployed.

**Methods:** Research articles till September 2018 are searched from Scopus by keywords as “4D printing” and “4D printing”<sup>”medical”</sup> and undertaken a bibliometric analysis of the identified papers. Further relevant papers were studied for application in the medical field.

**Results:** Search through Scopus identified 171 research articles on 4D printing and 13 research articles on 4D printing in the medical field. This study states that 4D printing is the latest technology that creates innovation and addresses complex medical problems. Paper briefly describes the 4D printing and details its difference from 3D printing technology. We have identified five steps to be used to create a medical model by using this technology and its prospective implementation for medical applications. Identified that research is carried out on 4D printing, but decidedly less publication is available in the medical field reporting the application of this technology. Finally, we have identified nine significant applications of 4D printing in the medical field. The main limitation is that it requires extensive investment & support for transformation.

**Conclusions:** 4D printing is to provide benefits to medical practitioners especially in the areas not covered by 3D printing technologies. 4D printing helps to create a 3D physical object by adding smart material layer by layer through computer-operated computer-aided design (CAD) data. It adds a dimension of transformation over time where printed products are sensitive to parameters like temperature, humidity, time etc. This technology can provide extensive support in the medical field, especially with better and smart medical implants, tools and devices. Now doctors and researchers can explore with 4D printing technology to provide better service to the patient.

### 1. Introduction

The review of the available literature identifies 4D printing as an advanced technique of 3D printing. Here changes in functionality, property and shape of a 3D printed product are a function of time. It seems to have the capability to achieve multi-functionality, self-assembly and self-repair. So, therefore, 4D printing can manufacture dynamic structure, adjustable shapes, with different properties or functionality. For this, 3D printing technique uses smart material and with an application of mathematical modelling for designing a structure.<sup>1,2</sup>

4D printing uses similar technology to that of 3D printing. It adds one more dimension of transformation over time, where printed product reacts with parameters like temperature/humidity etc. to change its form as per the requirements. It is a new & advanced technology, rapidly emerging through different disciplines; such as engineering, medical, material science, chemistry, basic sciences, computer science.

This technology is based on the fundamentals of stereolithography where ultraviolet light (UV) is used to cure a material layer by layer during the printing process.<sup>3–5</sup> It is a rapid and accurate manufacturing method of customised fabrication of soft structures. It uses unique materials which have self-deformation property and are adopted by scientists for research purpose.<sup>6–8</sup>

4D printing technology drives a significant transformation in the medical field. It has broader application in tissue engineering, chemotherapy and self-assembling human scale biomaterials. Now there is a development from 3D medical devices to 4D medical devices such as manufacturing of biomedical splint, stents, bioprinting and orthodontic devices. It manufactures implant as planned which, grows with human growth.<sup>9,10</sup> 4D printing handles such difficult situation easily with better accuracy. By the application of this technology, there are endless possibilities which potentially impact all sectors like medical, manufacturing and education. In the medical field, there is an excellent contribution of 4D printing technology to minimise the procedure of

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<https://doi.org/10.1016/j.cegh.2018.09.007>

Received 1 August 2018; Received in revised form 21 September 2018; Accepted 25 September 2018

Available online 26 September 2018

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surgery. For patient's body, doctors can use self-deforming component to treat any abnormality.<sup>11,12</sup>

In medical, there is a requirement to develop medical implant and devices which grown as per the patient growth. This technology can efficiently fulfil this requirement because the implants manufactured can change shape with time as the human body grown through the use of a smart material. In this process data of the patient is captured by Computer tomography (CT), Magnetic Resonance Imaging (MRI) and other scanning technologies which are easily printable by specialised machining technologies adding layer by layer techniques of intelligent medical material. This technology can develop new methods and material to create implants.<sup>13,14</sup>

In the medical field, doctors and researchers believe that 4D printing will evolve for the higher level of applications. It uses chameleonic materials in which, the material properties get changed according to temperature change. This technology will create a disruptive effect on medical and other related industries in the next upcoming years. It is an advanced material based technology with improved quality, efficiency, performance and is capable of producing medical implants and device of enhanced capabilities. It facilitates self-assembly of materials required to produced new products which further reduce the need for labour and speeds up the process.<sup>15–17</sup>

### 2. Comparative analysis of 4D printing takes over by 3D printing

Literature classifies 4D printing technologies into four main printing processes such as stereolithography, fused-deposition modelling, powder bed and inkjet head 3D Printing. These technologies are mainly dependent on material which has mechanical and thermal properties with higher flexibility.<sup>18,19</sup> In the future, it has great importance to redefine manufacturing-related industries which can augment the deficient areas of conventional manufacturing methods. Table 1 comparatively shows the evolution of 4D printing from 3D printing.

The fundamental difference between 3D printing and 4D printing is that 3D printing produces a static output which does not have a time element (dimension). For this process, a variety of materials, metals, powders, thermoplastic polymers, UV curable resins etc. are used. On the other hand, 4D printing uses only those materials which are temperature responsive, or humidity responsive, or pressure responsive etc. with the passage of time.

### 3. Research objective

In medical, there is a requirement of medical model which can change its shape in the human body with time or heat. The customisation is a significant challenge which is undertaken by 3D printing technologies. However, the medical model manufactured by 3D printing technique is rigid, and its shape remains same with time, the 4D printing technologies efficiently fulfil this requirement. Here with

**Table 1**  
Comparative analysis of 4D printing with the 3D printing.

S. No	Characteristics	3D Printing	4D Printing
1	Built Process	<ul style="list-style-type: none"> <li>3D printing repeats a 2D structure layer by layer from bottom to top</li> </ul>	<ul style="list-style-type: none"> <li>4D printing is the extension of 3D printing</li> </ul>
2	Material Used	<ul style="list-style-type: none"> <li>Uses thermoplastics, ceramics, metals, biomaterials or nanomaterials</li> </ul>	<ul style="list-style-type: none"> <li>Uses smart, multi-material and self-assembling material to build an object, which change its shape after getting manufactured</li> <li>There is a need to develop new materials as per the requirements of the applications</li> </ul>
3	Flexibility	<ul style="list-style-type: none"> <li>No flexibility, characterised by rigidity</li> </ul>	<ul style="list-style-type: none"> <li>Having flexibility, characterised by flexibility</li> </ul>
4	Object shape flexibility	<ul style="list-style-type: none"> <li>No flexibility, characterised by rigidity</li> </ul>	<ul style="list-style-type: none"> <li>Object shape is changed over time and with the change in temperature</li> </ul>
5	Programming of material	<ul style="list-style-type: none"> <li>Not use any programmable and advanced material</li> </ul>	<ul style="list-style-type: none"> <li>Use programmable and advanced (mostly new) material that can provide various functionalities</li> </ul>
6	Applications	<ul style="list-style-type: none"> <li>Its application is in medical, engineering, dentistry, automobile, Jewelry, toys, fashion, entertainment, aerospace, defence etc.</li> </ul>	<ul style="list-style-type: none"> <li>Dynamically changing configuration for all applications by 3D printing</li> </ul>

the use of a smart material, the shape of the product is not rigid, and it changes with time. Extensive research is happening to develop such materials and associated printing technologies suiting different applications.

For this, we need to study the status of research carried out by the 4D printing and identify the work undertaken by using 4D printing in medical. The study undertakes how 4D printing application will be applied in the medical field to fulfil various requirements and create innovation in this field.

### 4. Benefits of 4D printing over 3D printing

4D printing technology can develop products which can change characteristics and properties from environment change like temperature with time.<sup>20–22</sup> Various benefits of 4D printing are as follows:

**Capabilities of the printed smart products:** 4D printing provides a broad capability for users to print products with smart material which has broad applications in engineering, medical, dentistry and material science.

**Change of product shape as per the requirement:** Changes in the product shape of a 3D printed model related as a function of time where printed product reacts with the parameter like temperature, humidity etc. to change its form as per the requirement.

**Create innovation:** This technology innovates product during the design and development stage. The technology is also successfully used for research.

**Self-assembly:** This technology tends to produce a product which has self-assemble material property due to the usage of smart material.

### 5. The expected process to manufacture medical model using 4D printing technology

4D printing uses a digital CAD model to create a 3D physical model of smart material by adding layer by layer of material. Significant steps used by 4D printing in medical are as under:

#### Scanning and imaging

Various scanning technologies are used to capture a medical image; these technologies include CT, MRI, and scanners. These technologies are also used to analyse the defect and broken bone of the patient.<sup>13,23</sup>

#### Transformation of data into a digital 3D model

Scan data is essential to convert into a 3D model by using different software like OsiriX Imaging Software, 3D slicer, Mimics, Magics, 3D doctor, InVesalius. Before printing or design modification, it is essential

to have transform data into a 3D model.<sup>24,25</sup>

### Design modification and simulation

In the design modification step, various changes in the designing of medical implants and devices are undertaken as per the philosophy of the product design process. By using mechanical simulation, we can analyse the particular part of the body that it can be intended to perform the required function.<sup>26,27</sup>

### 4D printing

This undertakes the printing of medical implant by using smart materials layer by layer as per the required shape and size. This technology efficiently manufactures any complex shape medical devices and model as per the specific patient's anatomy. It provides excellent ability to fabricate an internal structure with higher flexibility.<sup>28,29</sup>

### Implementation of the printed model in surgery

Implants manufactured by 4D printing technology are used through actual implementation in the patient's body. This process makes surgery easy, successful and improves the reliability of surgery. After surgery patient could feel better due to the actual implantation smart material implant manufactured by 4D printing technology.<sup>10,30</sup>

## 6. Research status in 4D printing and 4D printing in medical

### 6.1. Research status in 4D printing

Research publications are increasing on 4D printing, taking data from Scopus by searching keyword as “4D printing”.; here we identified 171 articles published on this technology until September 2018. The first research article on 4D printing was published in 2007, in this year only one article published on this technology. In 2008, 2009, 2010, 2011, there was no single article published in these years. In 2012 and 2013, one article published in each year and 2014, there is an increment of publications and six articles. In 2015, thirteen, in 2016, twenty-six, in 2017, sixty-six and the year 2018 up to September, fifty-five articles were published on 4D printing. So we observed that research is growing fast in 2016, 2017 and current year 2018.

Various journals and sources published research articles on 4D printing. Out of some top journals publications, International journal of precision engineering and green manufacturing technology has the highest publications of nine. Smart materials and structures journal, and Virtual and physical prototyping journals both have same published eight articles each. ACS applied materials and interfaces have six publications, Assembly automation journal and Materials and design journal have both publications of five each. 3D Printing and additive manufacturing journal, and materials journal have published four papers each. Scientific reports journal published three research articles. Rest the journals and sources also published papers on 4D printing.

The engineering field gives maximum contribution of 27%, whereas “materials science” contributes 24%, ‘Computer science’ 12%, ‘Physics and astronomy’ 6%, ‘Chemistry’ also contributes 6%, ‘Energy’ 4%, ‘Business, Management and accounting’ also contributes 4% and there is also great contribution of 17% by ‘other fields’ that includes Chemical engineering, Mathematics, Biochemistry, Genetics and molecular biology, Medicine, Arts and humanities, Multidisciplinary, Environmental science, Social sciences, Decision Sciences, Pharmacology, Toxicology and pharmaceuticals.

### 6.2. Research status on 4D printing in the medical field

There is very less research available on “4D printing in the medical field”. By searching keywords as “4D Printing” “medical”, we obtained

only thirteen articles published until September 2018. In 2012 the first paper was published, no articles reported published in 2013 and 2014. In 2015, one article, in 2016, two articles, in 2017, three articles were published, and in the current year 2018 up to September, six articles are published in this field.

Different journals and source published articles on ‘4D printing in the medical field’. ‘ACS applied materials and interfaces’ and ‘Smart materials and structures’ both journals have published two papers each. Others journals and sources also published same publication of one in each; these include 3D printing and additive manufacturing, Journal of reconstructive microsurgery, Journal of thoracic disease, ‘Macromolecular materials and engineering’, Macromolecular rapid communications, Polimeri, Proceedings of SPIE the international society for optical engineering, Engineering and science advances.

In the area-wise contribution on “4D printing in medical field”, the maximum contribution of 33% is given by Materials science. Engineering contributes 15%, Computer science, Medicine, Physics and astronomy journals has an equal contribution of 11% by each field, Chemical engineering contributes 8%, Chemistry 7%, and Mathematics has 4% contribution by 4D printing technology.

From the Scopus data, we have analysed that there is some research is carried out on “4D printing”, but there are very few research articles published in “4D printing in the medical field”. Doctors and researchers can take advantages of this upcoming technology for the betterment of the medical field to provide excellent service and save the life of the patient.

## 7. 4D printing applications in the medical field

4D bio-printing is an emerging technique, where a time of usage is also integrated with a 3D bio-printing, in which printed medical model become capable of changing their shape and functionalities. This time-dependent shape model also provides a high potential for biomedical scaffolds and various another essential purposes. It has various emerging applications in medical, and Table 2 discusses important ones.

In medical, there is a requirement of accurate detail of anatomy which can improve clinical outcomes, shorten the effective length, reduce donor-site morbidity and decrease overall operative complications.<sup>47,48</sup> 4D printing has a high potential in biomedical applications like self-bending stents and other self-shrinking/tightening staples. 4D printing technology has a potential to change the surgeon approach for diagnostic and treatment planning in orthopaedics.<sup>49</sup>

## 8. Discussion

4D printing is the extension of 3D printing which is an innovative technique to manufacture smart medical implants and devices as per the patient's growth, by using a smart material. Data of patient is captured through CT, MRI and other scanning technologies and printed by 4D printing technology using the layer by layer technique. The implant can change shape according to time or as per the growth of the human body. It has excellent capability to manufacture stents and organs which can change the shape concerning time as per requirement. This technology can help save the lives of the patient and provide a better solution to severe organ shortages. It has exciting possibilities for tissue engineering and smart implants. 4D printing has explored its application for customising smart multi-material printing in medical to clearly show multi parts of the body in 3D printed model. It solves the breathing problem for babies with precise fit and perfect genetic match model of heart, kidney and liver with the higher flexibility of the printed material. 4D printing easily prints different smart medical tools and devices and has great possibilities to print skin graft like original colour. It is used for quite complicated surgery with a high success rate and save the life of the patient.

**Table 2**  
4D printing applications in the medical field.

S. No	Medical Application	Description	References
1	Smart stent	<ul style="list-style-type: none"> <li>● 4D printing could develop stents which can get expanded and take required shape with the help of heat of the patient body</li> <li>● This latest solution act quickly to save a patient's life for complicated surgery</li> </ul>	Zarek et al., 2016 <sup>10</sup> ; Bodaghi et al., 2018 <sup>29</sup>
2	Organ printing	<ul style="list-style-type: none"> <li>● A shape gets changed w.r.t time and temperature</li> <li>● This emerging technology applies to fabricate complex 3D organ</li> <li>● Used to print organs where own cells of the patient are applied and save a life</li> <li>● It is a promising solution for organ shortages</li> </ul>	Miao et al., 2017 <sup>30</sup> ; Saunders, 2017 <sup>31</sup>
3	Smart multi-material printing	<ul style="list-style-type: none"> <li>● Use UV curable polymer to layer by layer technique</li> <li>● It is a new process for printing customizable smart multi-material printing of medical implants</li> </ul>	Ge et al., 2016 <sup>14</sup> ; Akbari et al., 2018 <sup>32</sup>
4	Dyspnea (Breathing problem)	<ul style="list-style-type: none"> <li>● Clearly, show multi parts of the body in the 3D printed body</li> <li>● 4D printing technology save lives of babies which are suffering from Dyspnea (breathing problems)</li> <li>● It quickly creates a medical implant which can change shape over time as babies grew and helped them keep breathing</li> </ul>	Haq, 2015 <sup>33</sup> ; Choi 2015 <sup>34</sup>
5	Smart medical implants and tissue engineering	<ul style="list-style-type: none"> <li>● 4D printing creates exciting possibilities of the shape-shifting material</li> <li>● Its potential application could use for medical implants and tissue engineering that change their shape inside the body</li> <li>● Used for regeneration of those tissues where mechanical properties vary dynamically as our body gets active, such as muscle, bone, and cardiovascular tissues</li> </ul>	Hendrikson et al., 2017 <sup>35</sup> ; Mandon et al., 2017 <sup>36</sup>
6	Printing of heart, kidney and liver	<ul style="list-style-type: none"> <li>● In the future, 4D printing can print heart, kidney and liver by using the smart material</li> <li>● Ability to print these parts which have great flexibility with precise fit and perfect genetic match</li> </ul>	Yi et al., 2017 <sup>37</sup> ; Gosnell et al., 2016 <sup>38</sup>
7	Skin Graft	<ul style="list-style-type: none"> <li>● It has great possibilities to print skin graft like original colour of the patients</li> <li>● Also useful for the burn patient which will easily implant in the patient body and grows like an original</li> </ul>	Khoo et al., 2015 <sup>39</sup> ; He et al., 2018 <sup>40</sup>
8	Manufacturing of smart medical devices	<ul style="list-style-type: none"> <li>● This technology can manufacture 3D-printed complex smart medical devices which have excellent functional properties</li> <li>● Adjusted as per requirement of surgery concerning time</li> </ul>	Kuang et al., 2018 <sup>8</sup> ; Pei and Loh 2018 <sup>41</sup> ; Castro et al., 2017 <sup>42</sup> ; Zhao et al., 2018 <sup>43</sup>
9	Complex surgery	<ul style="list-style-type: none"> <li>● It could produce a haptic model to represent the movement of the body as well as appearance</li> <li>● In future, it can well be adopted for quite complicated surgery which is not possible by other manufacturing technologies</li> <li>● It can produce a model by using a smart material with the help of CT and MRI scan which accurately replicate hand or another body movement</li> <li>● It can represent anatomical details in a precise and accurate manner</li> </ul>	Chae et al., 2015 <sup>13</sup> ; Lee et al., 2017 <sup>44</sup> ; Javaid et al., 2018 <sup>45</sup> ; Sanjeet and Albert 2016 <sup>46</sup>

## 9. Future scope

In the future, 4D printing applications will increase in the medical field to fulfil the innovative requirements. It will become a ubiquitous and essential technology for the surgeon to fabricate smart, customised implantable medical devices that give efficient output. Through the use of a smart multi print model, it provides information about blood loss, blood clot; chest wound infection, and breathing difficulty. Due to its higher flexibility in the manufacturing of medical models, the surgeon can produce smart anatomies of the individual patient any time which was not previously possible. In future 4D printing technology will provide an essential improvement in medical, engineering and various other associated fields by the advancement of smart material. Objects printed by this technology could be helpful in engineering, automobile parts which are large and adjusted as per required environment condition and required power. In the plumbing system, these products can change the diameter of pipes as per flow rate and water demand. Pipes could have the possibility to automatically heal when there is any break or crack. This technology could also become the best solution for smart building and bridges which can be changed shape as per weather condition.

## 10. Conclusion

In upcoming years, 4D printing technology will create a disruptive effect in medical, engineering and other fields. It is a superior technique concerning with quality, efficiency and performance. In medical, every model is customised and vary from patient to patient which sourced from an individual patient can be printed easily in less time which has

extensive benefit to humanity. Research is growing on this disruptive technology. It provided extensive support in the medical field with better accuracy the manufacturing of customised smart implants, tools and devices. It replaces conventional scaffold fabrication methods, and the primary purpose of this technology is to fabricate implant with unique geometrical characteristics and feature with the higher flexibility to change the shape of the model. 4D printing technology drives a significant transformation in the healthcare sector like organ printing, tissue engineering and self-assembling human scale biomaterials. It creates a development of biomedical splint, stents, bioprinting and orthodontics devices as per human growth. In the future, this emerging technology will become more beneficial and help to create endless possibilities in the medical field.

## Conflicts of interest

None.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cegh.2018.09.007>.

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