



# Assessment of Knowledge and Understanding of Tissue Chip Mimicry's Impact on Dental Practice among Dental Practitioners: A Questionnaire based Study

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chips on sensors,  
microfluids

## ABSTRACT:

**Background:** Organ-on-chips have revolutionized various fields of research, including dentistry. These chips can be used to model oral tissues and study the interactions between teeth, gums, and other oral structures. By creating a realistic in vitro model of the oral cavity, researchers can investigate oral diseases, test new dental materials, and develop more effective treatments. These chips allow researchers to simulate the interactions between dental materials and oral tissues, providing insights into their long-term effects and potential risks.

**Aims:** The objective of this assessment study was to collect information about the knowledge and understanding of tissue chip mimicry's impact on dental practice among dental practitioners pan India.

**Materials and Methods:** A cross-sectional, self administered questionnaire-based study was conducted among 421 dental practitioners pan India. A pre-validated closed-ended questionnaire with 19 questions was given to collect the data under two headings: (a) knowledge of dental practitioners on 2D and 3D cell culture and (b) understanding of tissue chip mimicry and its role in dentistry. Results have been presented in numbers and responses for each of the questions have been reported as percentages.

**Result:** It is evident from the study that tissue chip technology is relatively new and to date, the emerging technologies have not found their way into widespread use.

**Conclusion:** Conducting long-term studies on organ-on-chip systems can provide valuable insights into the long-term effects of dental treatments and interventions. Encouraging collaboration between dentists, bioengineers, and material scientists can lead to innovative advancements in organ-on-chip technology for dental applications. Developing patient-specific organ-on-chip models can enable personalized dental treatments and interventions, improving treatment outcomes and patient satisfaction.

## INTRODUCTION

The science and technology of exact manipulation and processing of microscale fluids is known as microfluidics. It is generally used as a "lab-on-a-chip" to accurately manage microfluidic ( $10^{-9}$  to  $10^{18}$  L) fluids through micro channels ranging in size from tens to hundreds of microns <sup>[1,2]</sup>. Organ on chip is a

biomimetic system capable of simulating physiological organs and can regulate key parameters such as concentration fluctuations, shear force, cell patterning, tissue boundness or interactions between tissues. To simulate the physiological environment for human organs is a major objective of these chips <sup>[3-5]</sup>.



## Organs on Chips

Tissue chip mimicry is a revolutionary technique in dentistry that involves the development of artificial tissue models to mimic the structure and function of natural oral tissues [6]. These tissue chips are created using advanced bioengineering methods and can be used for various research purposes in dentistry.

- Drug testing
- Cell-cell interactions
- Cell-ECM studies
- Cell co culture
- Cancer cell metastasis
- Bacterial chemotaxis [7-9]

## Tissue Chip Mimicry and its relation with the Guardians of Dentistry

Organ-on-chips provide a more precise representation of human physiology compared to traditional cell cultures or animal models [1,10,11]. They provide a platform for studying organ-level physiology and disease mechanisms in a controlled laboratory setting [12-14]. Tissue chip mimicry has numerous applications in dental research, including:

**Drug Testing:** Tissue chips can be used to test the efficacy and safety of dental drugs, allowing researchers to study their effects on oral tissues without the need for animal or human subjects [15].

**Disease Modeling:** Tissue chips can be used to create disease models, enabling researchers to study the progression and mechanisms of dental diseases such as periodontitis and dental caries [16].

**Biocompatibility Testing:** Tissue chip mimicry can be used to test the biocompatibility of dental materials, such as fillings, crowns, and dental implants. By recreating the microenvironment of the oral cavity, researchers can evaluate how different materials interact with oral tissues and identify potential adverse reactions [8,17].

**Implant-Tissue Interactions:** Tissue chip models can simulate the interactions between dental implants and surrounding tissues, providing insights into the osseointegration process. This can help in the development of improved implant designs and materials, leading to better long-term success rates and patient outcomes [10,19].

**Oral Disease Research:** Tissue chip technology can aid in the development of new treatment strategies for oral diseases. By creating models that mimic the oral

mucosa, researchers can study the pathogenesis of conditions like oral cancer, periodontal disease, and oral infections [2]. This can lead to the discovery of novel therapeutic targets and the development of more effective treatments [9,12].

## Advantages

**Reduced Use of Animal Models:** Organ-on-chips offer an alternative to animal models in dental research and treatment. They can simulate the oral cavity and allow for the study of specific dental conditions without the need for animal testing, reducing ethical concerns and costs associated with animal research [20].

**Accuracy:** Tissue chip mimicry provides a high level of accuracy in replicating the structure and function of human tissue, allowing for more precise testing and analysis in dentistry [21,22].

**Reproducibility:** The ability to reproduce tissue chip models ensures consistent and reliable results, making it easier to validate research findings and develop effective dental treatments [23].

## Limitations

**Complexity:** Creating and maintaining tissue chip models in dentistry can be complex and require specialized expertise, equipment, and resources [15,18].

**Cost:** The cost of developing and using tissue chip models can be significant, making it a potential barrier for widespread adoption in dental research and practice [4,8].

## Study Design, Area, Duration and Population

A pre-validated cross sectional questionnaire study was conducted during the month of August through social media by sharing the desired questionnaire in various groups of Indian Dental Association of the states selected through random sampling pan India. Institutional Ethics Committee, KIMS, KIIT-Deemed to be University approved the study and clearance from the ethical committee with approval number KIIT/KIMS/IEC/1413/2023 was acquired for this research study. The primary goal of this study was to assimilate a complete analysis of the knowledge and understanding in the view of tissue chip mimicry's influence on dental practice in this modern era of nanotechnology. This survey was circulated to 421 dental practitioners pan India.



## Sample Size

The survey included 421 dental practitioners pan India. A total of 15 out of 29 states were selected randomly through lottery system to equalize our survey without any bias. The responses of 349 dentists were submitted in a total sample size of 421 and the response rate was 82.8%.

## Data Collection

Through online Google forms, participants were approached and invited to participate in the study. A comprehensive questionnaire based study was carried out to obtain data regarding dentist's knowledge and understanding about the impact of tissue chip mimicry in dental practice. The questions were developed in a multiple-choice pattern, allowing participants to choose the best response suited to them.

## Informed Consent

Participants were briefed prior to the survey about the aims and objectives and informed consent was taken via an option in Google forms.

## Questionnaire

The questionnaire was organized and divided mainly into two sections. A total of 19 questions were formulated to assess the knowledge and understanding of the dental practitioners.

*Section One:* Participants were asked to fill up the data regarding the state they belong to, in order to rule out the states which are not being included in the survey. Then a question was formulated to assess their awareness of the said topic. Response of those participants was counted who have awareness of tissue chip mimicry to rule out any bias in the responses.

*Section Two:* 18 questions were formulated in order to assess the knowledge and understanding of 2D and 3D cell culture and tissue chip mimicry and its application in dentistry.

## Data Analysis

The collected data was first entered into a data spreadsheet. For descriptive analysis, the data spreadsheet was put into IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp. Detailed analysis of the data is elaborated in the results below.

## Results

In answer to the question, "Are you aware of the term 'Tissue Chip Mimicry'?" out of 349 participants 187 replied yes i.e 53.6% were affirmative. (Figure 1.) Response of these 187 participants was included in the survey to eliminate any bias.

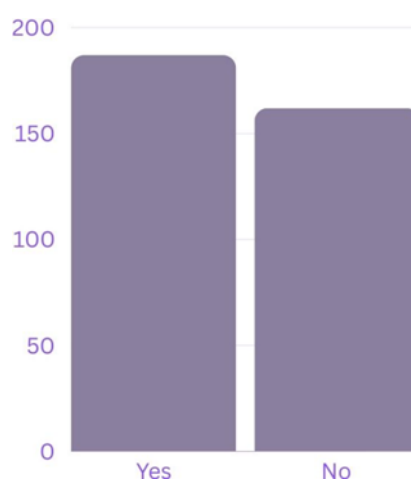


Figure 1.



Have you ever read articles or journals on tissue chip and how they work?

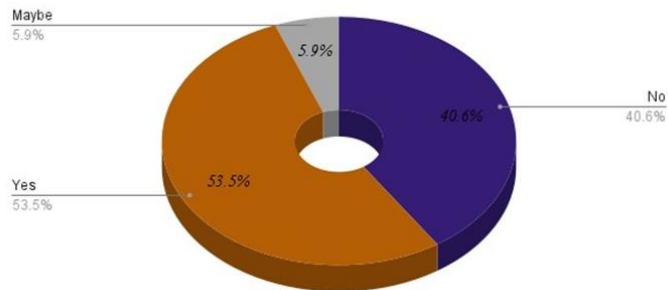


Figure 2.

Figure 2. demonstrates the distribution of participants those who have read about the ongoing research that is being done on organ on chips i.e 53.5% (n=100) have read articles and journals on it.

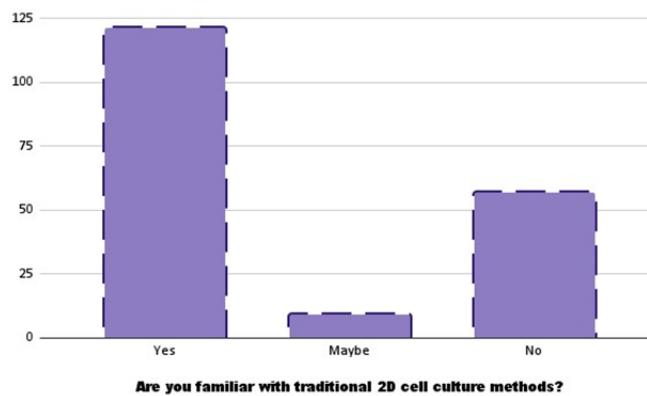


Figure 3.

Figure 3. illustrates the distribution of dental practitioners those who are familiar with 2D cell culture i.e 64.7% (n=121) are familiar with 2D cell culture where as 30.5% (n=57) are not familiar with it.

If so, do you think tissue chip mimicry compares to them?

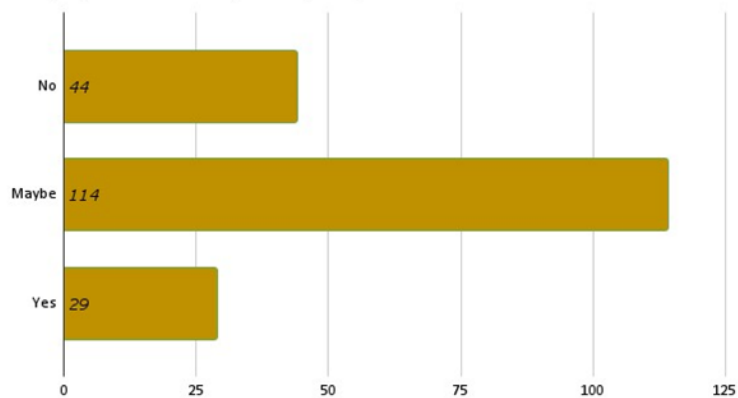


Figure 4.



Figure 4. represents that 61% (n=114) of the participants are not sure if tissue chip mimicry is equivalent to conventional 2D cell culture , 23.5% (n=44) are of the opinion that they are not similar and 15.5% (n=29) thinks that both 2D cell culture and tissue chip mimicry are same.

**Response to Knowledge based Questions**

As illustrated in Figure 5 , these questions were formulated to evaluate the knowledge on organ on chips.

As the findings shown in Table 1, 66.3% (n=124) of the practitioners were of the opinion that tissue chip mimicry can replace animal testing for various drug trials. 50.3%(n=94) of the participants are still unaware of the progress in this burgeoning field of nano-medico-technology. 47.1% (n=88) of the dental practitioners believe that tissue chip mimicry may raise some ethical concerns.

	Yes	No	Maybe
Do you believe that tissue chips can replace animal testing for drug development process and the pharmaceutical industry?	66.3%	5.3%	28.3%
Are you aware of any specific applications or research studies that have used tissue chip mimicry to advance our understanding of a particular disease or drug response?	15%	50.3%	34.8%
From an ethical standpoint, do you think tissue chip mimicry raises any concerns or considerations in dental treatment?	47.1%	21.9%	31%

Table 1

Figure 6. gives the impression that 36.4% (n=68) of dental practitioners have the opinion that tissue chip mimicry will be of more benefit to oral surgeons followed by 26.7%(m=50) thinks that it will be more helpful for the endodontists.

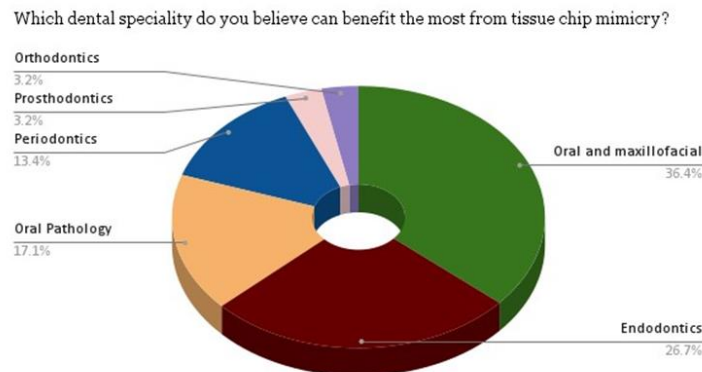


Figure 5.



Response to Application based Questions

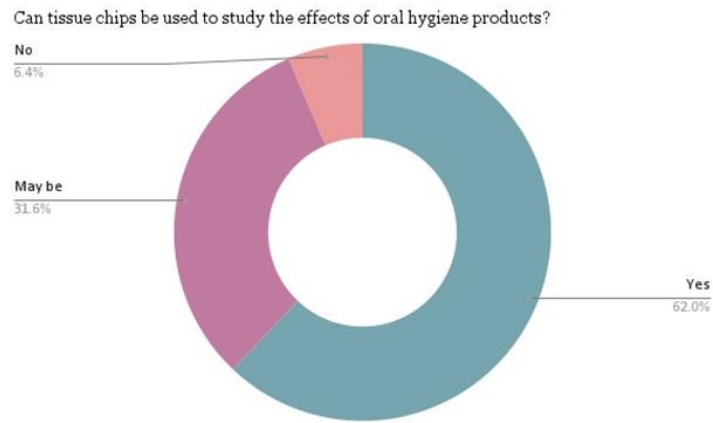


Figure 6.

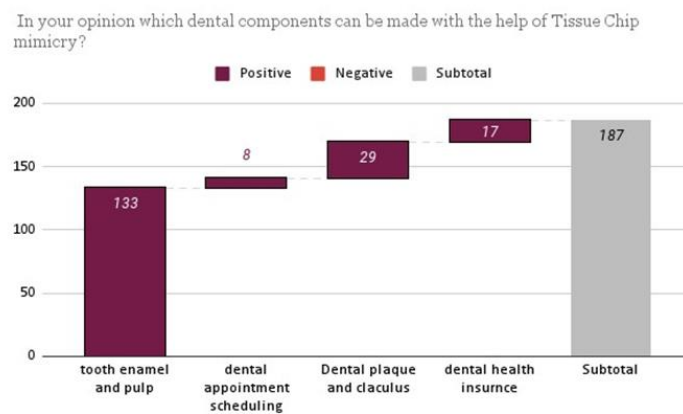


Figure 7.

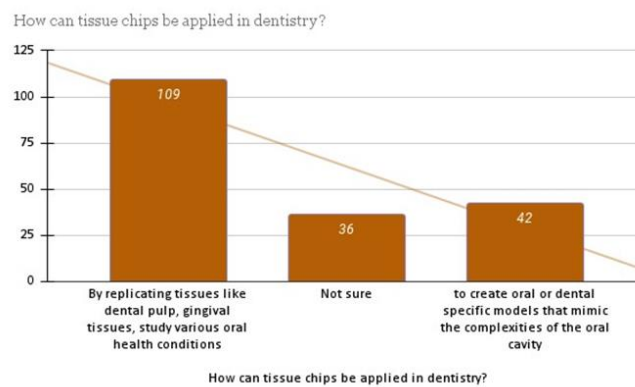


Figure 8.

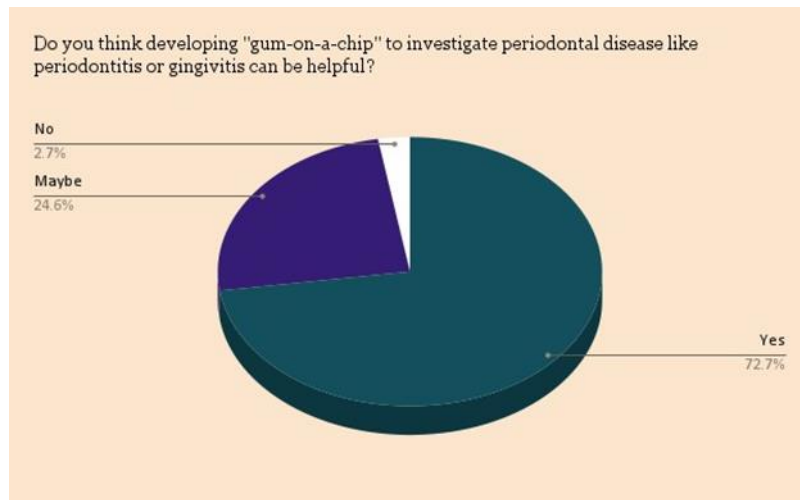


Figure 9.

Do you believe CAD CAM and 3D Printing aided with tissue chip mimicry can enable the fabrication of highly customized dental restorations?

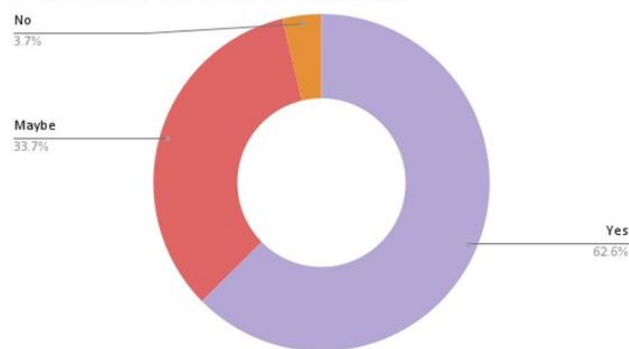


Figure 10.

Do you think they can be used for Personalized Medicine by using patients' own cells to create tissue chips to study how specific individuals may respond to treatments, leading to more tailored and effective therapies?

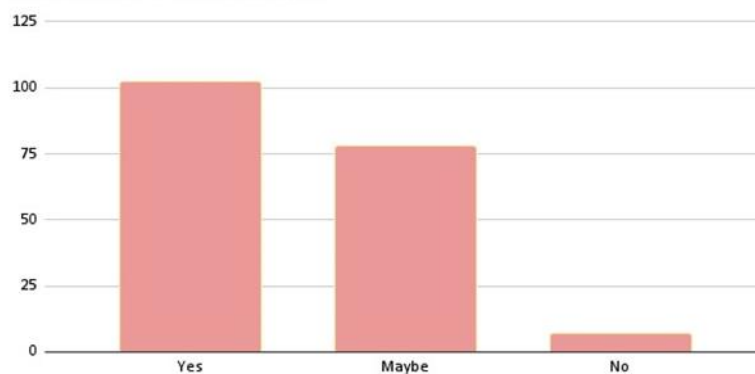


Figure 11.



This part contains six questions which aimed at eliciting dental practitioners' perspectives on tissue chip mimicry's applications in dental practice. *Figure 7* demonstrates that 62% (n=116) of dentists who have participated in the study think that tissue chip can indeed be used to study the effects of oral hygiene products on oral microbiota. Literature has it that tissue chip mimics oral physiology better and 58.3% (n=109) are of the opinion that these tissue chips can help us to study dental tissues like gingiva, dental pulp more intricately *Figure 9*. Lab on a Chip can be a more precise way to study about the complicated and the minute structure of periodontal ligament and this may facilitate a better understanding for the upcoming dentists and our study shows that 72.7% (n=136) of the dental practitioners belong to the same school of thought *Figure 10*. *Figure 11* gives us insight on the fact that 62.6% (n=117) of the dental practitioners are of the view that this recent development should be coupled with the digital dentistry i.e. CAD CAM and 3D bioprinting for a better patient work. During dental practice, dentists face a challenge as to know if a particular material suits the patient or not. There have been multiple cases of failed implants or prostheses, therefore this chip mimicry can be used as a study model for developing personalized medicine and more tailored therapies and in *Figure 12*, we see that 54.5% (n=102) of the dental practitioners are affirmative for the same.

## Discussion

The present study evaluated the knowledge and understanding of tissue chip mimicry and its impact on dental practice pan India. The findings gave us an opportunity to delve into the present scenario regarding its breakthrough.

A questionnaire-based cross-sectional study was conducted in the month of August by distribution of the Google forms in IDA Association groups of the randomly selected 15 states of India. Out of 421 participants, 72 participants did not give consent for the survey. The study proceeded with 349 participants. Among the 349 participants, the response of 162 participants was not included as they were unaware of the term tissue chip mimicry. This was done to eliminate any kind of bias in the survey.

In our study, awareness about 'Tissue Chip Mimicry' was evaluated and 53.6% of the studied population were

found to be aware of the term. The preference of tissue chip mimicry over animal testing among the studied population was found to be 66.3%. In the current study we assessed the knowledge of the studied population on tissue chip mimicry and 71.1% of the dental practitioners were of the opinion that this procedure can be used to study about tooth enamel and dental pulp<sup>[7]</sup>.

A noteworthy aspect revealed in the survey was that a significant portion of the studied population i.e. 72.7% wanted this technology to be used for more detailed study of parts of the oral cavity, 62.6% preferred it to be used with more technical applications like CAD CAM and 3D printing. While 102 participants (54.5%) appeared to prioritize this new arena to create better and more tailor-stitched personalized medications and therapies for their patients.

Dental practitioners may not have been exposed to or educated about tissue chip applications during their training. Traditional clinical techniques and procedures have often been emphasized in dental education and practice<sup>[20]</sup>. There may be a need for additional training and resources to incorporate cutting-edge technologies. Sometimes a difference in research and clinical practice can be significant. While tissue chip technology may be advancing in research settings, the translation of these advancements to routine clinical practice can be a gradual process.

## Future Directions

### Areas of Research and Development

**Enhancing Biocompatibility:** Continued research to improve the biocompatibility of tissue chip mimicry materials for better integration with the oral cavity<sup>[21]</sup>.

**Advanced Material Development:** Exploration of new materials and fabrication techniques to create more realistic and functional tissue chip models<sup>[16,22]</sup>.

**Microfluidic Systems:** Integration of microfluidic systems into tissue chip mimicry to simulate dynamic oral environments and enable more accurate testing<sup>[23]</sup>.

**Multidisciplinary Collaboration:** Encouraging collaboration between dentists, engineers, and biologists to drive innovation and accelerate the development of tissue chip mimicry in dentistry<sup>[11,14]</sup>.

## Conclusion

The use of tissue chips to simulate oral diseases, such as periodontal disease, dental caries or other oral health problems, could provide researchers and practitioners





with a look at the underlying mechanisms for these conditions. This could lead to more detailed understanding of disease development and the development of specific treatment options. Provide a facility for controlled environments where drugs are tested in terms of efficacy and safety. It would also be useful in dentistry to develop new medicines for conditions affecting the oral cavity, e.g. pain management and antimicrobials against dental infections. For the purposes of testing toxic effects in substances, including dental materials, tissue chips may be used. In this way, biocompatibility tests for materials applied in restorative and prosthetic dentistry might become more efficient. In order to give patients a comprehensive approach to care, tissue chip technology could be integrated with digital dental tools. The combination of the tissue chip study data with imaging and diagnostic technology may be part of this process. Incorporating tissue chip technology education into continuing education programs for dental professionals can be beneficial.

#### Key Findings

The research on tissue chip mimicry in dentistry has yielded several important findings:

Tissue chip mimicry has the potential to revolutionize dental procedures by providing more accurate and reliable results.

The use of tissue chips can significantly reduce the need for animal testing in dental research.

Tissue chip models allow for better understanding of the interactions between dental materials and human tissues, leading to improved treatment outcomes.

#### Implications for the Field

The findings of this research have significant implications for the field of dentistry:

Tissue chip mimicry can lead to the development of more advanced and personalized dental treatments.

The use of tissue chips can contribute to the reduction of animal testing and promote more ethical research practices.

Further research and development in tissue chip technology can lead to continuous advancements in dental care.

#### References

1. Singh, D., Mathur, A., Arora, S., Roy, S., & Mahindroo, N. (2022). Journey of organ on a chip technology and its role in future healthcare scenario. *Applied Surface Science Advances*, 9(Volume 9, June 2022, 100246), 100246. <https://doi.org/10.1016/j.apsadv.2022.100246>
2. Wu, Q., Liu, J., Wang, X., Feng, L., Wu, J., Zhu, X., ... Gong, X. (2020). Organ-on-a-chip: recent breakthroughs and future prospects. *BioMedical Engineering OnLine*, 19(1). <https://doi.org/10.1186/s12938-020-0752-0>
3. Esch, E. W., Bahinski, A., & Huh, D. (2015). Organs-on-chips at the frontiers of drug discovery. *Nature Reviews Drug Discovery*, 14(4), 248–260. <https://doi.org/10.1038/nrd4539>
4. Bhadriraju, K., & Chen, C. S. (2002). Engineering cellular microenvironments to improve cell-based drug testing. *Drug Discovery Today*, 7(11), 612–620. [https://doi.org/10.1016/s1359-6446\(02\)02273-0](https://doi.org/10.1016/s1359-6446(02)02273-0)
5. Breslin, S., & O'Driscoll, L. (2013). Three-dimensional cell culture: the missing link in drug discovery. *Drug Discovery Today*, 18(5-6), 240–249. <https://doi.org/10.1016/j.drudis.2012.10.003>
6. Knowlton, S., Yenilmez, B., & Tasoglu, S. (2016). Towards Single-Step Biofabrication of Organs on a Chip via 3D Printing. *Trends in Biotechnology*, 34(9), 685–688. <https://doi.org/10.1016/j.tibtech.2016.06.005>
7. França, C. M., Tahayeri, A., Rodrigues, N. S., & Ferdosian, S. (2020). The tooth on-a-chip: a microphysiologic model system mimicking the biologic interface of the tooth with biomaterials. *Lab on a Chip*, 20(2), 405–413. <https://doi.org/10.1039/C9LC00915A>
8. Hanks, C. T., Craig, R. G., Diehl, M. L., & Pashley, D. H. (1988). Cytotoxicity of dental composites and other materials in a new in vitro device. *Journal of Oral Pathology*, 17(8), 396–403. <https://doi.org/10.1111/j.1600-0714.1988.tb01304.x>
9. Huang, C., F Sanaei, & Wouter P. R. Verdurmen. (2023). The Application of Organs-on-a-Chip in Dental, Oral, and Craniofacial Research. *Journal of Dental Research*, 102(4), 364–375. <https://doi.org/10.1177/00220345221145555>
10. C.M. Ardila Medina, Jiménez-Arbeláez, G. A., & Annie Marcela Vivares-Builes. (2023). Potential Clinical Application of Organs-on-a-Chip in



- Periodontal Diseases: A Systematic Review of In Vitro Studies. *Dentistry Journal*, 11(7), 158–158. <https://doi.org/10.3390/dj11070158>
11. Curtis, M. A., Diaz, P. I., & Van Dyke, T. E. (2020). The role of the microbiota in periodontal disease. *Periodontology 2000*, 83(1), 14–25. <https://doi.org/10.1111/prd.12296>
  12. Makkar, H., Zhou, Y., & Kai Soo Tan. (2022). Modeling Crevicular Fluid Flow and Host-Oral Microbiome Interactions in a Gingival Crevice-on-Chip. *Advanced Healthcare Materials*, 12(6). <https://doi.org/10.1002/adhm.202202376>
  13. Jin, L., Kou, N., & An, F. (2022). Analyzing Human Periodontal Soft Tissue Inflammation and Drug Responses In Vitro Using Epithelium-Capillary Interface On-a-Chip. *Biosensors*, 12(5), 345. <https://doi.org/10.3390/bios12050345>
  14. Ahmed, T. (2022). Organ-on-a-chip microengineering for bio-mimicking disease models and revolutionizing drug discovery. *Biosensors and Bioelectronics: X*, 2022 Jul;100194(2022 Jul;100194), 100194. <https://doi.org/10.1016/j.biosx.2022.100194>
  15. Zhu, Y., Mandal, K., & Hernandez, A. (2021). State of the art in integrated biosensors for organ-on-a-chip applications. *Current Opinion in Biomedical Engineering*, 19(2021 Sep 1;19:100309-9), 100309–100309. <https://doi.org/10.1016/j.cobme.2021.100309>
  16. Sun, W., Luo, Z., & Lee, J. (2019). Organ-on-a-Chip for Cancer and Immune Organs Modeling. *Advanced Healthcare Materials*, 8(15), 1900754. <https://doi.org/10.1002/adhm.201900754>
  17. Rios, A. C., & Clevers, H. (2018). Imaging organoids: a bright future ahead. *Nature Methods*, 15(1), 24–26. <https://doi.org/10.1038/nmeth.4537>
  18. Saglam-Metiner, P., Gulce-Iz, S., & Biray-Avci, C. (2019). Bioengineering-inspired three-dimensional culture systems: Organoids to create tumor microenvironment. *Gene*, 686(2019 Feb;686:203–12), 203–212. <https://doi.org/10.1016/j.gene.2018.11.058>
  19. Jang, Y., Jung, J., & Oh, J. (2023). Bio-Microfabrication of 2D and 3D Biomimetic Gut-on-a-Chip. *Micromachines*, 14(9), 1736. <https://doi.org/10.3390/mi14091736>
  20. Figeys, D., & Pinto, D. (2000). Lab-on-a-Chip: A Revolution in Biological and Medical Sciences. *Analytical Chemistry*, 72(9), 330 A-335 A. <https://doi.org/10.1021/ac002800y>
  21. Gorjikhah, F., Davaran, S., & Salehi, R. (2016). Improving “lab-on-a-chip” techniques using biomedical nanotechnology: a review. *Artificial Cells, Nanomedicine, and Biotechnology*, 44(7), 1609–1614. <https://doi.org/10.3109/21691401.2015.1129619>
  22. Neužil, P., Campos, C. D. M., & Wong, C. C. (2014). From chip-in-a-lab to lab-on-a-chip: towards a single handheld electronic system for multiple application-specific lab-on-a-chip (ASLOC). *Lab Chip*, 14(13), 2168–2176. <https://doi.org/10.1039/c4lc00310a>
  23. Nima Farshidfar, Assar, S., & Mohammad Amin Amiri. (2023). The feasible application of microfluidic tissue/organ-on-a-chip as an impersonator of oral tissues and organs: a direction for future research. *Bio-Design and Manufacturing*, 6(4), 478–506. <https://doi.org/10.1007/s42242-023-00235-5>