Integrating Active Learning, Case Studies, Cytotoxicity Testing, and Ethical Considerations in Biomaterials Education: A Novel Approach

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Abstract:

This study presents a new active learning approach designed to enhance the educational experience in a biomaterials class through the incorporation of device case studies, a cytotoxicity testing experiment, and ethical considerations. Traditional biomaterials courses often lack hands-on experiences that bridge theoretical knowledge with practical application, limiting students' ability to grasp the real-world implications of their studies. To address this gap, we implemented a multifaceted pedagogical strategy that integrates active learning principles, laboratory experimentation, and ethical discourse.

The active learning modules were centered around case studies of biomedical devices and a cytotoxicity testing experiment. The case studies approach was to have the students address a given set of questions about material selection, device design and testing of a medical device with recommendations for improvement. Active learning activities were incorporated into the class to help students to address these questions. The lab experimentation provided students with a hands-on opportunity to assess the biological impact of various biomaterials. Through this experiment, students gained practical skills in experimental design, data analysis, and interpretation, fostering a deeper understanding of biomaterials beyond theoretical concepts. The inclusion of ethical considerations in the biomaterial curriculum was addressed through a debate. This encouraged students to reflect on the societal implications of biomaterials research, fostering a sense of responsibility and ethical awareness among future practitioners.

The study employed both qualitative and quantitative assessment methods, including pre- and post-module surveys, and academic performance evaluations. The survey instrument captured students' self-assessment of their knowledge of medical device fundamentals, device design and device testing at the beginning and at the end of the course. The survey instrument also captured students' perceptions toward the various active learning components introduced into the course. Results indicated a significant improvement in students' confidence, engagement, and understanding of biomaterials concepts. Surveys also show that out of the four types of active learning strategies introduced, three were highly successful. Majority of students either agree or strongly agree that the case study component (88%), lab component (88%), and the ethics debate (78%) played an important role in their learning process. 52% of the students found the literature survey activity useful. Additionally, the final reports highlighted the positive impact of the ethical discussions on students' awareness of the broader implications of biomaterials research.

This innovative educational approach contributes to the ongoing discourse on effective teaching methods in biomaterials education and provides a blueprint for educators seeking to enhance student learning outcomes.

INTRODUCTION

An engineer is the professional who designs, invents, and creates tools of human development. Hence, mastery of an engineer over technical knowledge and its practice is crucial not just for the individual but often for the development of entire societies. As the Italian architect Stefano Marzano once said “"*every time we design a product we are making a statement about the direction the world will move in*" [1]. As engineering instructors, we must strive to create well-rounded engineers, who are technically sound, creative designers, with strong ethical convictions. Engineering education in the United States has traditionally emphasized the acquisition of technical knowledge [2]. Traditional engineering courses can often lack the hands-on training that bridge theoretical knowledge with practical application, limiting engineering students' ability to grasp the real-world implications of their studies [2]. To address this gap, we need to configure engineering courses to include, in addition to technical and contextual knowledge, competency of practice, laboratory and design experiences, while emphasizing professionalism and ethics.

Anecdotal data as well as experimental evidence have shown that students learn better by constructing their knowledge, rather than by passively receiving knowledge. The vital point here is that the students need to be ‘active’ participants in the process of learning. Significant number of studies have shown that active learning pedagogy can successfully enhance student learning [2 - 9]. Activities, such as laboratory work, have been shown to offer significant gains in learning outcomes across various disciplines. These activities involve hands-on experiences that allow students to formulate hypotheses, collect data through experiments, and interpret results [10, 11]. Active learning allows for much more interaction among students, as well as between students and instructors. Time in the class is set aside for students to process what they are learning, discuss with others, and apply their knowledge to real life scenarios. On the spot assessment and feedback can be provided to the students as they work through the course material in groups or individually.

Case based learning (CBL) is an established approach in STEM education. Students can gain knowledge by working through real-world situations with guided questions and discussions [10-15]. This work aims to show that case studies can be further enhanced by incorporation of active learning modules that support the discussion questions.

Study Goal: This approach aims to use a medical device case study combined with active learning to improve knowledge acquisition and engineering design confidence in a Biomaterials class. Our specific learning objectives are:

1. Students should be able to recommend, assess, and critique medical device material components
2. Students should be able to determine and describe the ethical implications of material choice and usage in a medical device.
3. Students should be able to select appropriate biocompatibility tests for a medical device once given the usage parameters
4. Students should be able to design a cytotoxicity assay with appropriate controls once given the materials and physical aspect of the medical device.

EXPERIMENTAL DESIGN

BME 2210, *Biomaterials: Foundations and Application in Medicine* was a previously lecture-only required course taught to biomedical engineering majors in their junior year. The course comprises of three modules. Module 1 focuses on the chemical properties of biomaterials used in the health industry. Module 2 focuses on biomaterial degradation, mechanical, and surface properties of biomaterials, and how these properties can be altered to design better biomaterials. Module 3 explains how the human body reacts to biomaterials and how biomedical engineers work around these constraints to design effective and safe medical appliances.

In a redesigned version of this course, which ran over 2 years, a multifaceted pedagogical strategy was implemented that integrated active learning modules such as group literature survey, laboratory experimentation, and ethical discourse into the course (Figure 1).

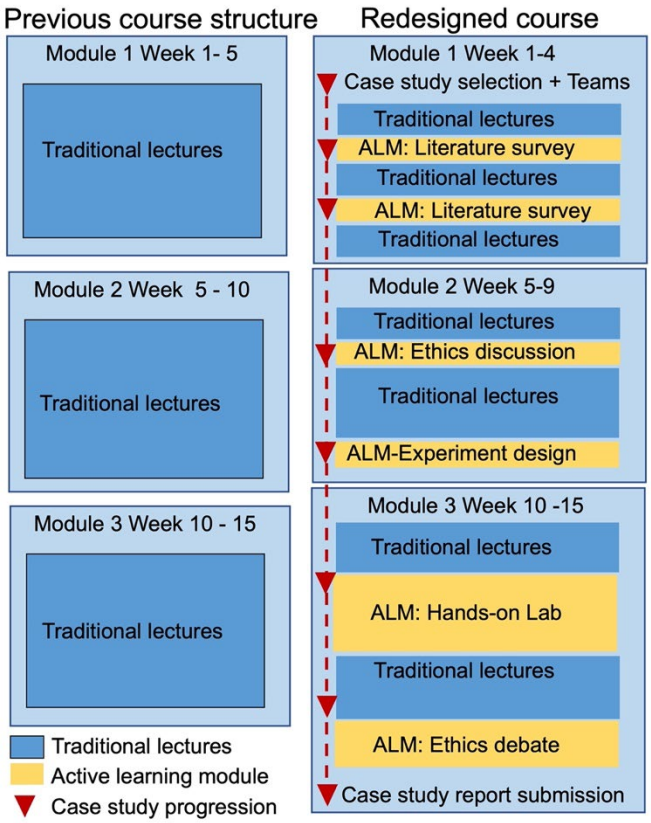

Figure 1. Comparison of redesigned course and the original biomaterials course. Active learning components are included as indicated

Student teams worked on medical device related case studies. Four case study options were provided, each related to a medical device. The options were artificial hip joints (AHJ), intraocular lenses (IOL), blood bags, and intrauterine contraceptive devices (IUD) respectively. Each student selected their case study, post selection, students with the same choice were grouped into teams of 3-4. Each case study consisted of a set of questions about biomaterial selection, testing, and ethical implications of using the material in that particular device. The case study questions can be found in Appendix A. Active learning modules (ALM) were created specifically to address these questions. The class size for the redesigned course was 62 in Year 1 and 67 in Year 2. There were no significant changes in the running of the course from year 1 to year 2.

The class was taught once a year in the Fall semester. The following active learning strategies were implemented in the two years of the class.

Literature Survey Discussion:

To address the questions of material choice and mechanical/chemical properties of the device students were asked to do a scientific literature review on the device. During the class period they discussed their findings with all the groups having the same device.

Ethics Discussion:

Each case study contained a question that required students to explore ethical aspects of the biomaterials used in their medical device. Towards the middle of the semester, concepts of engineering ethics were introduced to the students via an ethics lecture and discussion in class. Specifically, during this lecture, students were acquainted with the National Society for Professional Engineers (NSPE) Code of Ethics for Engineers. The instructor presented a brief summary of the fundamental canons of the code of ethics, focusing on the canon that states that engineers shall '*hold paramount the safety, health, and welfare of the public*'. Students were then asked to discuss their ethics related case study question (Appendix A) with their group members and arrive at a resolution using this canon for guidance. Teams were asked to submit a statement/paragraph describing their team's final resolution.

At the end of the semester a class debate was held where student teams defended their team resolution. In the debate, teams presented their evidence backed arguments and included their conclusions from the debate in their final case study report.

Biocompatibility Discussion:

Biocompatibility is a key question in the choice of materials for a medical device. The active learning laboratory consisted of students undertaking a cytotoxicity assay that would allow them to gain hands-on experience with the required biocompatibility tests for their case study device. Students were first given a lecture that covered the biocompatibility tests recommended by the FDA for different applications [16]. A table taken from the FDA website was used as well as a discussion of the "ISO 10993-1: Biological evaluation of medical devices – Part 1" standard. A key learning objective was for students to be able to choose the appropriate biocompatibility tests based on the device and its usage through the "nature of body contact" and "contact duration". This concept was reinforced by providing biomedical device examples and soliciting discussion on what tests should be chosen. Also covered in the lecture was the fact that the cell cytotoxicity assay is required for all body-contacting medical devices [17]. The three cytotoxicity assays (extract, direct contact, and indirect contact) were presented as well as what criteria should be used to determine the best assay for the device. ISO 10993-5: Biological evaluation of medical devices – Part 5: Tests for *in vitro* cytotoxicity was discussed as well as use of appropriate controls and methods to assess cytotoxicity.

Cytotoxicity Assay Design:

In order for students to apply the material presented in lecture, student groups were asked to provide a draft protocol for a liquid elution (extract) assay for their case study material. The liquid elution cytotoxicity assay was chosen since it was the most convenient based on length of lab time, type, and availability of materials to be tested. They had to provide stepwise instructions on how they would perform the assay, as well as how much material is needed, timing, controls, and method of assessing cell viability, and cytotoxicity level.

Summary of Hands-on Experimental Procedure:

Student case study groups performed the cytotoxicity assay on their device material over two weeks in 1 hour lab sessions/week. Students placed sterile test materials in liquid media for 24 hours at 37^{o}C. During this time any toxic components in the test article can diffuse into the culture medium. L929 cell cultures were grown in a near confluent monolayer in 12 well plates

by teaching assistants (TAs). The medium from each well was removed and replaced with liquid media that had been exposed to the test material. The 12 well plates were incubated for 24 hours at 37ºC after which the students examined the cells under a microscope for morphological changes. They then stained the cells with trypan blue and counted them to assess the degree of cell death due to the sample material.

The materials used in the cytotoxicity assay were titanium to represent the artificial hip joint; silicone hydrogel to represent Intra-ocular lens; polyvinyl chloride to represent blood bags and copper/polypropylene to represent IUDs. The controls were: positive control – latex and negative control -high density polyethylene (HDPE). A table detailing these materials can be found in Appendix B.

The cells used in the cytotoxicity assay were L929 rat fibroblasts and the media was DMEM with 1% Penicillin/Streptomycin + 10% Fetal Bovine Serum.

Students performed a qualitative evaluation on the cells after exposure to the medium by viewing them under a microscope and assigning a cytotoxic grade (0-4). The grade is based on an estimated percent lysis (death) and on the morphology (appearance) of the cells. Test materials pass the assay if the cytotoxic score is ≤ 2 ($\leq$ 50% lysis). For the assay to be confirmed, the negative controls (HDPE) must have a grade of 0 (reactivity none) and the positive controls must have a grade of 3 or 4. The cytotoxicity score table can be found in Appendix C.

DATA COLLECTION AND ANALYSIS

The overall effectiveness of the study was determined by assessment methods approved by the institutional **IRB protocol number # IRB0145662**. Surveys were designed and administered by the authors. At the beginning of the course students were given a pre-survey where they were asked to self-assess their knowledge of medical device fundamentals, device design, and device testing. The same survey (post) was given at the end of the course. As well as the pre-questions, the end of semester survey contained 4 additional questions on the effectiveness of the four active learning modules. Both surveys can be found in Appendix D. While the surveys weren't validated, the students were given a rubric to use when assessing their knowledge or level of confidence. This rubric can be found in Appendix E.

In addition, students were given pre and post surveys directed to the learning objectives of the lab activity. Before the lab module students were given a survey consisting of Likert scale and short answer questions asking them about their confidence level in designing and working with biocompatibility and medical devices. The survey can be found in Appendix F. The same survey was given 4 days after the lab activity had finished.

Statistical analysis was performed on the pre and post data as well as between the responses from the 2 years. Pre and post-survey responses from the same participants underwent a paired two tailed t-test to understand changes or differences between the two sets of responses. In addition, a Cohen's D test was used to calculate effect sizes which will indicate the magnitude of the differences observed between the pre and post-survey data. Any p-values obtained from the t test with $p<0.05$ were considered statistically significant.

Quantitative assessment to determine the success of the '*Ethics discussion'* ALM was done by evaluating the ethics write-up included by the student teams in their final case study report. To measure the level of understanding of ethical considerations among students, a two-step evaluation was performed on the student submissions. First, it was assessed whether students had taken pertinent topics into consideration in their discussion, for example, health equity with respect to accessibility of blood bags and eye care devices, environmental impact of biomaterials, safety and regulatory practices during manufacture and recycling of biomaterials etc. Second, it was evaluated whether their arguments were adequately backed by evidence. The student submissions were assigned the follow grades based on the parameters stated below.

- *'Very Good'*: Student team explains ethical issue clearly using references and provides a clear conclusion of ethical use of biomaterial with reference to the device.
- *'Satisfactory'*: Student team explains ethical issue but does not provide adequate evidence to back their conclusions.
- '*Poor*': Inadequate information/data. Lacks evidence and clear assessment.
-

Assessments were performed by the instructor, the co-author of this study.

To analyze student understanding of the cytotoxicity assay, an exam question that tested the achievement of the lab learning objectives was assessed. The report and exam question were evaluated with rubrics that graded various indicators of quality and student understanding. The exam question and rubrics can be found in Appendix G. The report rubric for the case study report can be found in Appendix H.

Course evaluations provided an indirect assessment of the laboratory and active learning modules.

RESULTS

Students were asked four questions at the beginning and end of the semester to assess their knowledge of 1. Testing of medical devices; 2. Design of medical devices; 3. Manufacturing of medical devices and 4. Materials used in medical devices (Appendix D). Figure 2 shows how student response to each question changed from the beginning to the end of the semester for years one and two respectively. This change was found to be significant based on a t-test ($p = 1.4x10^{-29}$) and Cohen's D analysis. In both years, at the end of the semester we see an increase in the percentage of students that assess their knowledge level as being above average and/or exceptional in the various aspects in the field of Biomaterials.

The end of semester survey allowed us to assess the effectiveness of the active learning modules. As seen in Figure 3, three out of four types of active learning modules were highly successful in creating perceived improvement of learning among students. The majority of students either agree or strongly agree that the experimental design component (88% in year 1, 90% in year 2), hands-on laboratory component (88% in year 1, 86.7% in year 2), and the Ethics debate (78% in year 1, 81.7% in year 2) played an important role in their learning process. 52% of the students found the literature survey activity useful in year 1, while 58.3% found it helpful in year 2.

Figure 2. Student self-assessment of knowledge in biomedical devices and biomaterials in pre and post surveys over two years. Number of students, n = 62 (Year 1), n = 67 (Year 2). Student response rate 95.1% (Beginning and end of Year 1), 89.6% (Beginning and end of Year 2).

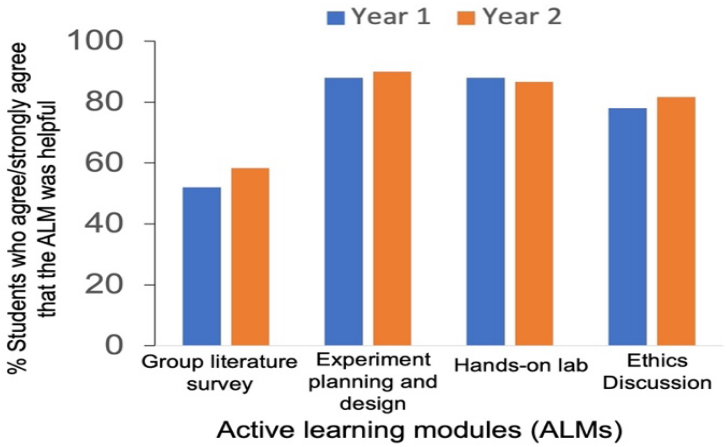

Figure 3. Student assessment on the effectiveness of the Active Learning modules. Number of students, n = 62 (Year 1), n = 67 (Year 2). Student response rate 95.1% (Year 1), 89.6% (Year 2)

The effectiveness of the active hands-on lab component in building confidence in cytotoxicity assays and biocompatibility testing is shown in Figure 4. Results from the self-assessment survey showed that students mean value of confidence in their cytotoxicity and biocompatibility knowledge increased by 35% (Pre 30% – Post 65%). This change in confidence was found to be statistically significant. The t-test analysis showed p values < 0.05 (1.6E-14) and Cohen D values ranging from 1.7 -1.9. The results from Year 1 and Year 2 were found to be similar (no statistical difference, p = 0.7).

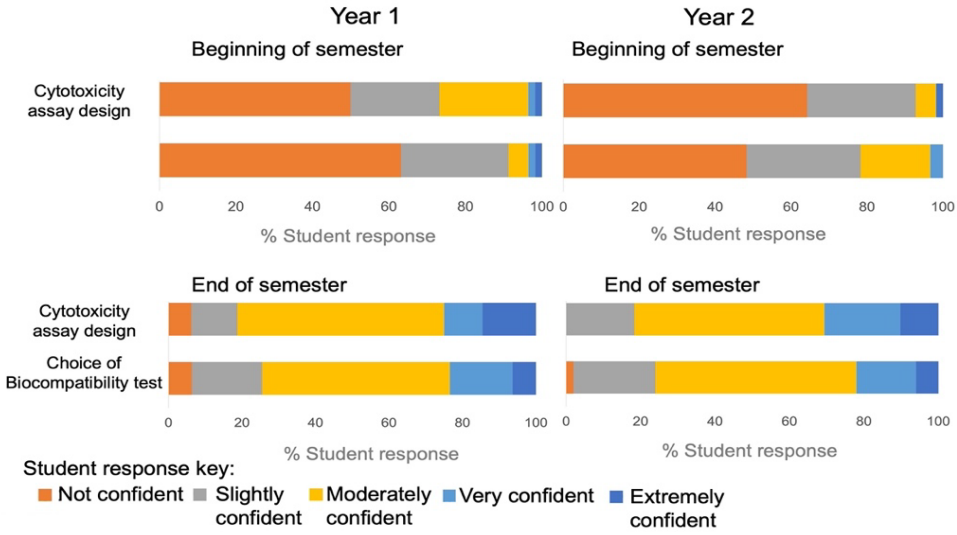

Figure 4. Student self-assessment of confidence in cytotoxicity and biocompatibility knowledge over two years. Number of students, n = 62 (Year 1), n = 67 (Year 2). Student response rate 100% (Beginning, Year 1), 85% (End, Year 1), 98% (Beginning, Year 2), 80% (End, Year 2).

The students in both years were able to successfully complete the cytotoxicity assay lab activity. Figure 5 shows the images of the L929 cells after exposure to the respective test materials. Student groups made conclusions on their test materials using images such as in Figure 5 and the cytotoxicity score chart.

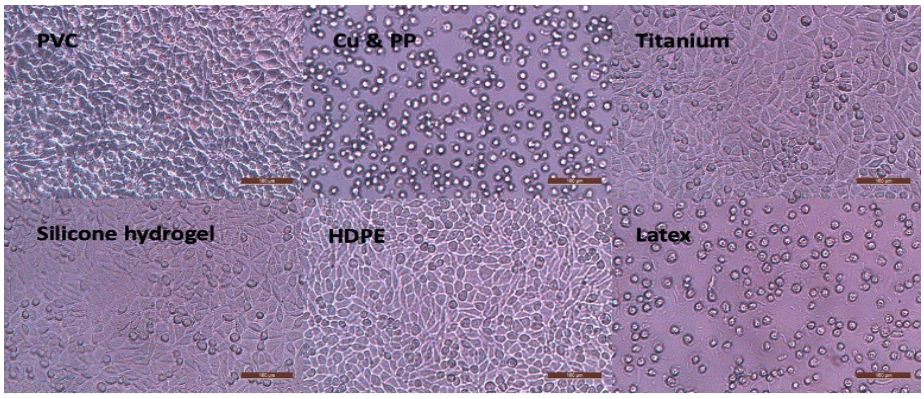

Figure 5. Student microscope images of L929 cells after exposure to soaked material media.

Table 1 shows the class combined average cytotoxicity score for each material.

Material (Device)	**Average Cytotoxicity Score**	**Conclusion**
Titanium (AHJ)	1.6 ± 0.5	Not cytotoxic
Silicone hydrogel (IOL)	1.6 ± 0.5	Not cytotoxic
PVC (Blood bag)	1.8 ± 0.4	Not cytotoxic
Copper and Polypropylene (IUD)	3.8 ± 0.4	cytotoxic
Latex (+ve control)	4.4 ± 0.5	cytotoxic
High Density Polyethylene (-ve control)	0.4 ± 0.5	Not cytotoxic

Table 1. Average +/- St. Dev. of class cytotoxicity scores for each material

Student performance on an exam question was used to assess how they well they achieved learning objectives 3 and 4. Figures 6, 7, and 8 shows the % of students who had an excellent, adequate and poor grasp of the concepts of biocompatibility testing (Learning objective 3) and cytotoxicity assays (Learning objective 4) as well as use of controls. A full description of how the student work was evaluated is given in Appendix G.

Overall these results showed that the learning objectives were achieved. 80% of students in year 1 and 88% in year 2 were able to pick appropriate biocompatibility tests when given the usage of a biomedical device. 90% of students in year 1 and 93% in year 2 were able to justify the choice of the cytotoxicity assay. There was no statistical difference in Years 1 and 2 on how students answered the exam question with respect to biocompatibility tests and choice of assay. However, student's knowledge and use of controls improved in Year 2. Figure 8 shows that only 33% in Year 1 knew the controls and why they were needed in a cytotoxicity assay. In Year 2, 83% showed competency in the use

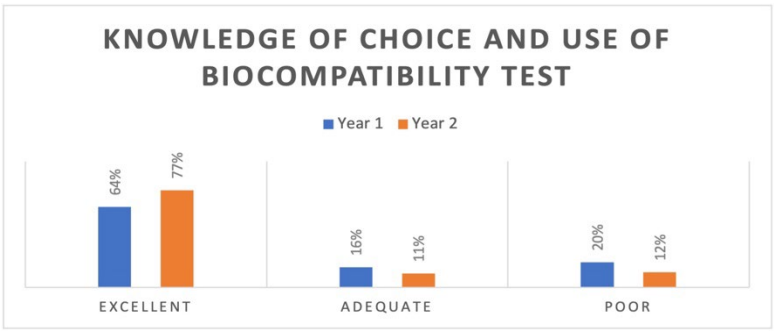

Figure 6. Students performance in exam question assessing biocompatibility.

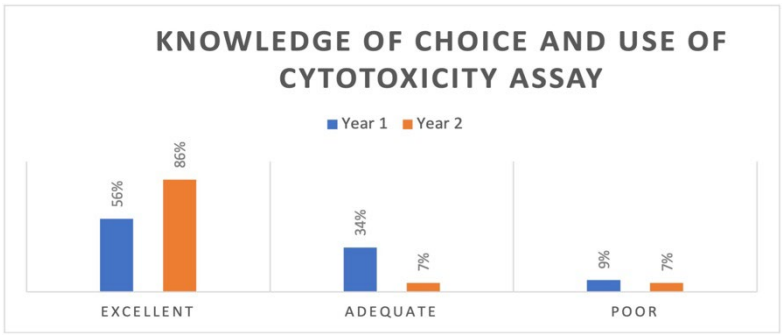

Figure 7. Students performance in exam question assessing cytotoxicity

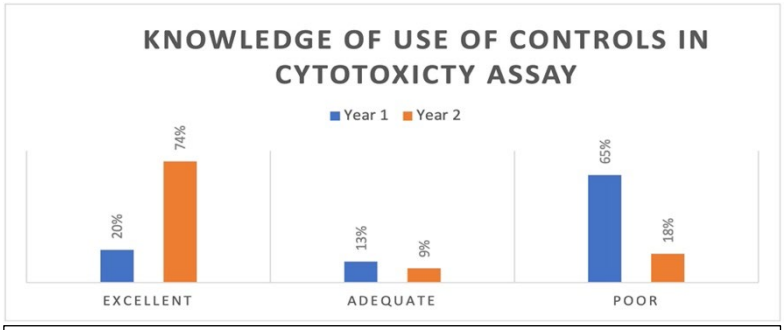

Figure 8. Students performance in exam question assessing use of controls.

and purpose of controls. This improvement can be attributed to the discussion on the significance of experimental controls with the instructor during the on lab period. The specific role of various controls used in the experiments was discussed extensively during the laboratory session.

The case study culminated in a group project report that addressed answers to the questions posed in Appendix A. It also included an ethical discussion of the use of the material, and the cytotoxicity assay results for their material. Figures 9 and 10, show the performance of the students in both years.

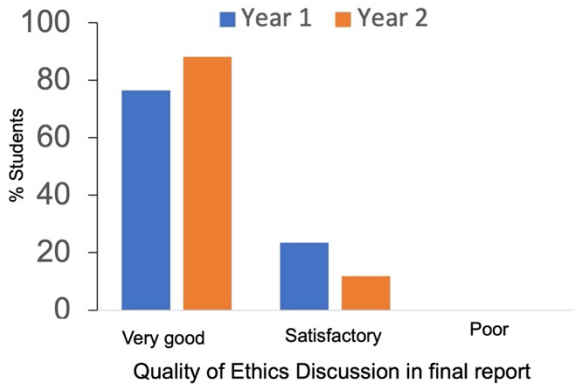

Figure 9. Students performance in the Ethics discussion included in their final report.

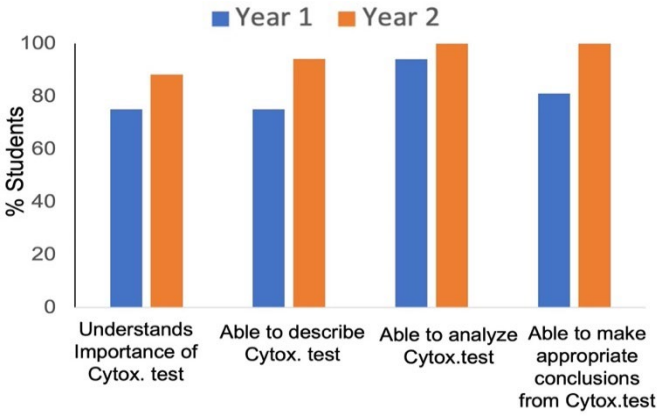

Figure 10. Students who had a satisfactory performance in case study report with respect to the cytotoxicity assay

The percentage of student teams that exhibited a very good performance in their final ethics related question was much higher than students that exhibited satisfactory performance. No team exhibited poor performance.

Figure 10 shows that students were able to successfully distill their knowledge and results of the cytotoxicity assay and incorporate it into the final report. In both Years 1 and 2 at least 70% of students were able to describe the importance of the cytotoxicity assay on device design, describe the assay, interpret the results, and provide appropriate conclusions. There was no statistical difference in their ability to understand, describe and analyze the cytotoxicity test from Year 1 to Year 2. The evaluation criteria and rubric are described in Appendix H.

Course evaluations indicate that students enjoyed the course with the active learning modules and thought it enhanced their learning (Table 2)

Year-1	Year-2
Active learning modules "*made the class more engaging and interactive*" *"The active learning modules, especially the lab ones were very useful"*	*"I really enjoyed the active learning module of the course. I felt as though the final paper did provided a great platform to ultimate synthesize everything we had learned. We had to consider biocompatibility, surface and mechanical properties, as well as ethics when choosing biomaterials to design a medical*

"Strengths of this course included the in-person cytotoxicity lab we conducted. I enjoyed the hands-on experience we got."	*device. The course felt exceedingly relevant to my career as a biomedical engineer."* *"Final project was really interesting, I wish we devoted more time to it. Maybe longer debates or debates across multiple days"*

Table 2. All student comments related to the active learning modules from end of year course evaluations.

DISCUSSION AND CONCLUSIONS

In conclusion, our study demonstrates the effectiveness of integrating active learning modules and case study-based learning to enhance student learning in a Biomaterials course. Through a structured approach, we observed significant improvements in students' ability to recommend, assess, and critique medical device material components, meeting our intended learning objectives. Our findings are supported by studies such as Deslauriers et al. (2019) and Ballen et al. (2017) [4, 18] where both papers have demonstrated that active learning methodologies lead to increased student learning and performance.

The utilization of case studies allowed us to expose students to real-world issues governing the manufacturing and application of medical devices, fostering a deeper understanding of the complexities within the biomaterials field. This is similar to other applications of case studies in engineering where students explored complex, discipline specific problems and developed appreciation of actual engineering scenarios in industry [19, 20]. Moreover, by incorporating an active learning module featuring in-class debates, we facilitated meaningful discussions on engineering ethics in the context of biomaterial usage in the medical industry.

Furthermore, the inclusion of a laboratory experimentation module provided students with valuable hands-on experience in assessing the biological impact of various biomaterials. This practical component not only enhanced students' experimental design skills but also strengthened their abilities in data analysis and interpretation, thereby extending their comprehension beyond theoretical concepts as shown in the final report.

In summary, the integration of active learning, laboratory experimentation, and ethical considerations not only enriches the educational experience but also equips students with the necessary skills to navigate the complex ethical landscape inherent in the field of biomaterials. By incorporating active learning components to teach key engineering concepts, we propose a pedagogical approach that encourages and empowers students to critically analyze data and work with real-life problems in the Biomaterials domain. This holistic approach prepares students for the multifaceted challenges they will encounter as future engineers in the biomaterials industry.

STATEMENT OF ETHICAL REVIEW AND HUMAN SUBJECT RESEARCH:

The surveys and methodology of this study were approved by the IRB at Cornell University (IRB protocol number # IRB0145662).

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Acknowledgements: This work was supported by a Cornell College of Engineering McCormick Teaching Excellence Initiative CRISTEL grant (Course Redesign Initiative to Support Engaged Learning).

Case Study- 1: Artificial hip joint.

In this case study you will look at the material selection for hip prostheses and highlight mechanisms for corrosion of metals in the body.

- Describe the components of an artificial hip joint and select the biomaterials you will use to make each part based on material
  - Biocompatibility
  - Mechanical properties
  - Surface properties

- Discuss the mechanisms of corrosion of metal parts that constitute hip prostheses.

- Using experimental data you collected in lab, hypothesize why release of metals into the body from hip prosthesis is a major limitation. Provide a novel approach to how you may prevent corrosion in prostheses

- Comment on the following statement. "*Mining process of metals like titanium will involve the removal of vegetation cover and topsoil which might lead to severe erosion with eventual serious impact on the population but these metals are required to improve (AHJ, IUD) and sometimes preserve (pacemakers) human life*."

Assessment
The word limit for the paper is 2000 words (**not** including figures, tables, figure legends, and references). The report should be typed, double spaced, you are free to include figures and tables. You must include full references for all your sources (web addresses for web sites, and all authors, journal etc. for papers). You should number your references and cite the number as the reference in the text. Information from scientific papers must be included.

Resources
Sources of information include

- The scientific literature (see Web of Science, PubMed etc.)

Here are some articles to get you started:

Bradberry SM, Wilkinson JM, Ferner RE. (2014) Systemic toxicity related to metal hip prostheses. Clin Toxicol (Phila). 52(8):837-47

Pezzotti G, Yamamoto K. (2014) Artificial hip joints: The biomaterials challenge. J Mech Behav Biomed Mater. 31:3-20

- Online magazines, e.g. Orthopedics Today
  https://www.healio.com/news/orthopedics/current-issues/orthopedics-today

- Information from manufacturers.

- USPTO
  https://www.uspto.gov/trademarks-application-process/search-trademark-database

- Other resources
  https://www.nlm.nih.gov/archive//20040831/pubs/cbm/hip-repl.html

Case Study- 2: The Blood Bag Case Study

This case study involves discussing the biomaterial science and processing of plastics, as well as the effects of plastics on blood products.

Perform the following tasks

- Discuss the history of blood bags
    - Glass bottles were initially used for storing whole blood. Americans began to use plasticized PVC bags in the Korean War, circa 1950. Since 1990 other polymers have been considered. Expand and comment.

- Discuss the mechanical, optical, and thermal properties of polymers relevant to blood bags.
    - Hint: Polymers can be transparent (if a single-phase glass) or translucent (if 2-phase semi-crystalline with light scattering). Polymers may exhibit high flexibility (low bending stiffness) so that one can squeeze the bag.

- In a blood bag a polymer material is interacting with living blood cells. Using the data you collected in the lab comment on biocompatibility of this biomedical device.

- Address the following question. "*Will you use a polymer that is more environmentally friendly but much more expensive, to create blood bags, knowing that this may make the device less accessible to patients belonging to lower socio-economic backgrounds".*

Assessment
The word limit for the paper is 2000 words (**not** including figures, tables, figure legends, and references). The report should be typed, you are free to include figures and tables. You must include full references for all your sources (web addresses for web sites, and all authors, journal etc. for papers). You should number your references and cite the number as the reference in the text. Information from scientific papers must be included.

Resources
Sources of information include
- The scientific literature (see Web of Science, PubMed etc.)

Here are some articles to get you started:

Carmen, R. (1993) The Selection of plastics materials for blood bags. Transfusion medicine reviews, 7.

Al Salloum H, Saunier J, Dazzi A, Vigneron J, Etcheberry A, Marlière C, Aymes-Chodur C, Herry JM, Bernard M, Jubeli E, Yagoubi N. (2017) Characterization of the surface physico-chemistry of plasticized PVC used in blood bag and infusion tubing.

Mater Sci Eng C Mater Biol Appl. 75:317-334.

- Information from manufacturers.

- USPTO
https://www.uspto.gov/trademarks-application-process/search-trademark-database

- Other resources
http://www.aabb.org/tm/Pages/highlights.aspx

Case Study- 3: Intra-ocular lenses case study

This case study looks at polymer material used for Intra-ocular lenses, their design, and biocompatibility issues.

Perform the following tasks.

- Describe what are intra-ocular lenses and how do they work. Pick a polymer and discuss what properties of this particular polymer makes it a suitable biomaterial for intra-ocular lenses. (Hint: Discuss optical properties and response to the environment within the human body)

- Enumerate some complications that may arise from intra-ocular lenses use and what precautions are in place to prevent these.

- Discuss the safety tests that need to be performed by manufacturers before a lens is brought to the market. Also describe the results of the laboratory tests you performed that are part of this process.

- Address the following question. "*Will you use a polymer that is more environmentally friendly but much more expensive, to create intra-ocular lenses, knowing that this may make the device less accessible to patients belonging to lower socio-economic backgrounds".*

Assessment
The word limit for the paper is 2000 words (**not** including figures, tables, figure legends, and references). The report should be typed, you are free to include figures and tables. You must include full references for all your sources (web addresses for web sites, and all authors, journal etc. for papers). You should number your references and cite the number as the reference in the text. Information from scientific papers must be included.

Resources
Sources of information include

- The scientific literature (see Web of Science, PubMed etc.)

Here are some articles to get you started:

Werner L (2008) Biocompatibility of intraocular lens materials. Current Opinion in Ophthalmology, 19: 41–49

Costerton JW, Montanaro L, Arciola CR. (2005) Biofilm in implant infections: its production and regulation. Int J Artif Organs. 28(11):1062-8.

- Information from manufacturers.

- USPTO

https://www.uspto.gov/trademarks-application-process/search-trademark-database

- Other resources

https://www.aao.org/eye-health/diseases/cataracts-iol-implants
https://www.uofmhealth.org/health-library/hw36086

Case Study- 4: Contraceptive Intrauterine Device (IUD) case study

This case study looks at the properties of material used in Contraceptive Intrauterine Device (IUD), their design, and biocompatibility issues.

Perform the following tasks.

- Describe the historical evolution of the engineering design of IUDs and how the design contributes to its functional purpose.

- Discuss the mechanical properties of the polymer material used in IUDs and why these properties need to be considered while making these devices.

- Discuss how the material components of the IUD may interact with its environment within the human body. Use the results from your laboratory experience to make your case.

- Comment on the following statement. "*Mining process of metals like copper will involve the removal of vegetation cover and topsoil which might lead to severe erosion with eventual serious impact on the population but these metals are required to improve (AHJ, IUD) and sometimes preserve (pacemakers) human life*."

Assessment
The word limit for the paper is 2000 words (**not** including figures, tables, figure legends, and references). The report should be typed, you are free to include figures and tables. You must include full references for all your sources (web addresses for web sites, and all authors, journal etc. for papers). You should number your references and cite the number as the reference in the text. Information from scientific papers must be included.

Resources
Sources of information include

- The scientific literature (see Web of Science, PubMed etc.)

Here are some articles to get you started:

Chen Y, Luo Y, Jia Z, Jia D, Chen J. (2014) Preparation and characterization of silicone rubber/nano-copper nanocomposites for use in intrauterine devices. Biomed Mater Eng. 24(1):1269-74.

Roylance D. (1993) Assessment of olefin-based IUD tail strings. J Appl Biomater. 4(4):289-301.

- Information from manufacturers.

- USPTO
https://www.uspto.gov/trademarks-application-process/search-trademark-database

- Other resources
https://www.unfpa.org/sites/default/files/resource-pdf/IUDbook_finalwlinks_042911.pdf

Appendix B

Materials used in the cytotoxicity assay

Medical Device	**Material**	**Source**	**Sterilization Technique**
Artificial Hip Joint	Titanium	Titanium pieces (Sigma-Aldrich)	Autoclave
Intra-ocular lens	Silicone hydrogel	Commercial contact lens	Pre-sterilized
Blood bag	Poly Vinyl Chloride	Blood bag	70% Ethanol
Intrauterine device	Copper and Polypropylene	IUD prototype	Autoclave
Controls			
Positive control	Latex	Latex gloves	70% Ethanol
Negative control	High Density Polyethylene	HDPE sheets	Autoclave
Untreated (media) control	DMEM media	DMEM Media	Pre-sterilized

Appendix C

Score of Cytotoxicity Assay based on morphological analysis

Grade 0	Cells are confluent, stretched out, and attached
Grade 1	20% rounding and some reduced confluency (low reactivity)
Grade 2	50% rounding and reduced confluency (mild reactivity)
Grade 3	70% rounding substantially reduced confluency (high reactivity)
Grade 4	Nearly complete destruction

Appendix D

BME 2210 Beginning of Semester Survey.

Your Name:

Preferred pronoun:

How would you rate your **current** knowledge of biomaterials (Metals, Ceramics, and Polymers)?

1. Non-existent
2. Rudimentary
3. Average
4. Above average
5. Excellent

How would you rate your **current** knowledge of manufacturing of biomedical devices?

1. Non-existent
2. Rudimentary
3. Average
4. Above average
5. Excellent

How would you rate your **current** knowledge of design of biomedical devices?

1. Non-existent
2. Rudimentary
3. Average
4. Above average
5. Excellent

How would you rate your **current** knowledge of testing of biomedical devices?

1. Non-existent
2. Rudimentary
3. Average
4. Above average
5. Excellent

What is the one biomedical device that you want to know more about, and why?

BME 2210 End of Semester Survey.

Your Name:

Preferred pronoun:

Knowledge assessment

How would you rate your **current** knowledge of biomaterials (Metals, Ceramics, and Polymers)?

6. Non-existent
7. Rudimentary
8. Average
9. Above average
10. Excellent

How would you rate your **current** knowledge of manufacturing of biomedical devices?

6. Non-existent
7. Rudimentary
8. Average
9. Above average
10. Excellent

How would you rate your **current** knowledge of design of biomedical devices?

6. Non-existent
7. Rudimentary
8. Average
9. Above average
10. Excellent

How would you rate your **current** knowledge of testing of biomedical devices?

6. Non-existent
7. Rudimentary
8. Average
9. Above average
10. Excellent

Additional comments on knowledge acquirement:

Active learning module assessment

The journal discussion module improved my understanding of scientific research related to Biomaterials.

1. Strongly disagree
2. Disagree
3. Neutral
4. Agree
5. Strongly agree

The cytotoxicity protocol design module improved my fundamental understanding of testing of Biomedical devices.

1. Strongly disagree
2. Disagree
3. Neutral
4. Agree
5. Strongly agree

The hands-on lab module improved my understanding of testing of biomedical devices.

1. Strongly disagree
2. Disagree
3. Neutral
4. Agree
5. Strongly agree

Group discussions made me aware of underlying ethical aspects of biomedical engineering.

1. Strongly disagree
2. Disagree
3. Neutral
4. Agree
5. Strongly agree

Additional comments on the active learning modules:

Teamwork experience

Working in a team helped my learning

1. Strongly disagree
2. Disagree
3. Neutral
4. Agree
5. Strongly agree

Please include your team number here _____

I was the leader of the team.

1. Yes
2. No
3. We didn't have a leader

If you answered 'Yes' to the question above, please describe your experience as. We are especially interested in learning about challenges and how you were able to surmount them.

If you answered 'No' to the question above, please describe why you decided not to become the leader. Looking back would you change your decision.

If you answered 'We didn't have a leader' to the question above, please describe why your team decided not to have a leader. Looking back do you think it was the right decision.

Please comment on any additional challenges you faced while working as a team.

Appendix E

We are requesting that you complete the following survey. This is not a graded assignment. We will use the information to create relevant course content.

https://cornell.ca1.qualtrics.com/jfe/form/SV_afm4hhheNXq2aiOLinks to an external site.

NOTE: If you need a reference for the scale, this is a suggestion:

Non-existent - Never heard of 'it'.

Rudimentary - Heard about 'it' but don't know much about it.

Average: Heard about 'it' and know some general facts about 'it'.

Above average - Heard about 'it', know a great deal.

Excellent - Heard about 'it', know a great deal about 'it'. Feel ready to apply this knowledge to solve engineering problems.

APPENDIX F

BME 2210 Pre and Post-Survey (2022&2023)

Start of Block: Default Question Block

Q1 Please rate how familiar you are with the topic of biocompatibility

- Not familiar at all (1)
- Slightly familiar (2)
- Moderately familiar (3)
- Very familiar (4)
- Extremely familiar (5)

Q2. What test do all biomaterials that come in contact with the body have to undergo?

_____

Q3 You are building an implant that is made up of various materials, is the FDA more interested in the biocompatibility of each material or the whole device?

- The whole device (1)
- Each individual component (2)

Q4 If you were given a medical device and told its use in a patient, how confident would you be in identifying which biocompatibility tests are needed before clinical use?

Not confident				Moderately confident						Very Confident
0	10	20	30	40	50	60	70	80	90	100

Level of confidence ()	

Q5 If you were given a new material that will be used on the surface of a patient's skin, how confident would you feel designing a test in the lab to assess the cytotoxicity of the material?

0 10 20 30 40 50 60 70 80 90 100

level of confidentce ()	

APPENDIX G

Question. Your company has designed a small device made of silicon, polyethylene, and copper wires that delivers a constant dose of a drug for 30 days when placed under the skin. (10 Points total)

A) Please list all the biocompatibility tests that needs to be performed on this device to receive FDA approval and state why so many tests are needed. (4 Points)

B) You need to assess the cytotoxicity of the device, which cytotoxicity testing method would you choose and why? (2 Points)

C) Describe the principle behind the viability method you used to assess the cells after exposure to the cytotoxicity test. (2 Points)

D) Please list the controls used in the cytotoxicity test. Describe the purpose of all the controls. (2 Points)

Solution KEY:

A) The tests needed are cytotoxicity, sensitization, irritation, systemic toxicity, sub-chronic toxicity, genotoxicity and implantation. (3 Points, 0.5 point for each test the student provides). So many tests needed because the device will be implanted in tissue for 30 days and the FDA (ISO -10993-10) guidelines dictate the tests needed for such conditions.(1 point)

B) Because the device has many different materials and it is small, **the liquid elution test** would be best since it will **assess the whole device with all its parts**. It is also **easy to perform**. (2 Points)

C) The viability assay used was trypan blue staining. Trypan blue is a dye that is generally called a live/dead stain. The principle is that a cell can only take up this dye if it is dead (1 point). If a cell is alive the membrane is intact and cannot take up the dye. If a cell is dead the membrane is not intact and the dye can be taken up by the cells and will show blue under a microscope (1 point).

D) Negative Control- High Density Polyethylene (0.5pts); Positive Control – Latex (0.5 pts). The control samples are needed to provide known validated response to the cytotoxicity assay, near complete destruction for the positive control and high confluency for the negative control. The controls ensure that the experimental process is not flawed and can be used as a comparison for the sample results (1 point).

The score for Question A was used to plot Figure 6.
The score for Question B was used to plot Figure 7.
The score for Question D was used to plot Figure 8.

Grading Rubric for each section of question

Excellent:	For answers scoring 80 -100% of the total points
Adequate:	For answers scoring 50 - 80% of the total points
Poor:	For answers scoring 0-50% of the total points

Appendix H

Students included the cytotoxicity testing in the final report on their medical device. Their report was assessed in the following criteria:

Criteria	**Criteria is satisfied if**
Importance of the Cytotoxicity test	Students describe that the cytotoxicity assay is a required test for all biomedical devices and there are 3 types of assays. Students justify the use of the liquid elution test for their material.
Describe the Cytotoxicity test	Students present a well described methodology of what they did in the lab with appropriate volumes, temperature, incubation times, and materials. They include description of the controls.
Able to analyze the cytotoxicity data	Students present their data clearly, these include images and cytotoxicity score. Students process their cell count data (live/dead data) to provide viability data.
Able to make appropriate conclusions	Students make a conclusion based on all the data on whether their material is cytotoxic. Students comment on what other biocompatibility tests are needed based on the use of their device and discussed the controls.