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# Application and evaluation of virtual simulation technology in 'corneal contact lens' education

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## Abstract

**Background** To evaluate the impact of the corneal contact lens virtual simulation teaching system on students' course experience and self-directed learning in 'corneal contact lens' education.

**Methods** This study developed a virtual simulation experimental teaching system for 'corneal contact lens' education. A longitudinal comparison of the course experience and self-directed learning abilities of the same group of students at a university in Fujian Province before and after using the system was conducted through questionnaires. Pearson correlation analysis was used to determine the correlation between factors of course experience and self-directed learning abilities before and after the application of the virtual simulation experimental teaching system.

**Results** A total of 290 valid questionnaires were collected from 145 optometry undergraduates (71 males, 74 females, average age  $21.05 \pm 0.82$  years). Students completed questionnaires before and after using the virtual simulation teaching system. The evaluation of teaching improved from 4.05 to 4.45, basic skills mastery increased from 3.49 to 4.40, and overall course experience rose from 3.07 to 4.17. The system significantly enhanced self-directed learning abilities ( $P \leq 0.05$ ), with increased scores in teacher role expectations (3.91 to 4.41), independence (3.03 to 4.34), learning confidence (3.02 to 4.35), learning process evaluation (2.89 to 4.33), and learning strategy use (3.37 to 4.36). However, correlation analysis revealed a significant decrease in the correlation between students' confidence in learning ability, process evaluation, and strategy use after utilizing the virtual simulation technology.

**Conclusion** Virtual simulation technology not only significantly enhanced students' experience in corneal contact lens courses but also improved their self-directed learning abilities. It changed students' cognition and behavior patterns regarding the learning process to some extent, providing new pathways and possibilities for the innovation and development of digital education in ophthalmology.

**Keywords** Virtual simulation technology, Corneal contact lenses, Orthokeratology lenses, Digital education

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## Introduction

By 2050, it is projected that 4.758 billion people worldwide will be myopic, with 938 million classified as highly myopic, underscoring a significant rise in global myopia prevalence [1]. In response, corneal orthokeratology lenses and peripheral defocus-adjustable contact lenses are increasingly being used to control myopia progression in children [2, 3]. As a result, “Corneal Contact Lens Science” has become a core compulsory course in optometry education.

Traditionally, corneal contact lens education is taught through a combination of lectures, textbook-based learning, and limited clinical practice. Students are often constrained by the lack of access to a mount of real patients, inadequate experimental conditions, and minimal hands-on opportunities, which restricts their ability to fully master practical skills in fitting and evaluating contact lenses [3]. As a specialized and highly practical branch of ophthalmology and optometry, corneal contact lens science is essential in the training of optometry professionals. However, current digital laboratory teaching resources are severely limited. The advent of Virtual Simulation Technology (VST) presents new opportunities for reforming corneal contact lens education.

VST, is a technology that generates a virtual environment through computer technology, allowing users to interact with it. It utilizes various technical means such as 3D graphics, animation, sound, and tactile feedback to create an immersive virtual world where users can perform various operations and experiences [4]. This technology has wide applications in various fields, especially in medical education. For instance, through virtual simulation anatomy teaching software, students can observe and manipulate various systems and organs of the human body in detail, conduct 3D anatomical studies, understand complex human structures, and perform various cutting and separation operations to enhance their understanding of anatomy and physiology [5]. VST-based surgical virtual simulation systems can effectively improve the surgical performance of young physicians and help beginners master surgical techniques in a short time [6]. Additionally, VST can be used for evaluation in medical education. Through virtual exams and assessment systems, students can test their knowledge and skills in a virtual environment, and teachers can provide evaluations and feedback based on their performance [7]. Sikder et al. [8] proposed that simulators based on VST can effectively measure performance, distinguish skill levels among trainees, and improve surgical skills and patient outcomes in cataract surgery. Despite these advances, research on the application of VST in ophthalmology teaching, particularly in corneal contact lens education is still relatively limited.

This study developed a new virtual simulation laboratory teaching system for ‘corneal contact lens’ education. The primary aim is to evaluate the effectiveness of this system by comparing students’ course experiences and self-directed learning abilities before and after its implementation.

## Methods

### Virtual Simulation teaching system development and application

To implement VST in the ‘corneal contact lens’ course, a feature-rich teaching system was developed. This study used personalized and intelligent corneal orthokeratology fitting as an example, designing the system operation process based on students’ learning behaviors (Fig. 1).

Integrating clinical fitting needs for both soft and hard corneal contact lenses, the system incorporates intelligent parameter selection programs and deep learning-based clinical fitting evaluation algorithms. The virtual simulation teaching system for corneal orthokeratology fitting, which is a single system used throughout the course, includes the following 13 modules (Fig. 2). Before beginning the modules, students received a dedicated class session to learn how to operate the VST system and understand the workflow of each module. Students could then study the required knowledge through pre-reading and video tutorials at their own pace. The VST system was accessible online, enabling students to engage with the modules flexibly, without time or location constraints, and practice repeatedly using different cases.

#### Module 1 system interface login module

Students log into the teaching system through the system interface. Upon logging in, the system provides detailed operating instructions and learning objectives to help students familiarize themselves with the system and clarify the goals of their current learning session. This module lays the foundation for subsequent learning, guiding students to operate the system, understand course content, and achieve learning objectives.

#### Module 2 knowledge testing module

The Knowledge Testing Module is where students undergo a basic knowledge assessment. Upon passing the test, they can proceed with case selection and lens fitting modules. If they do not pass, they are required to review the foundational knowledge before retaking the test. After reviewing and consolidating knowledge, students enter the knowledge testing module to ensure they have mastered the relevant knowledge. Upon passing the test, students can return to the staged case selection module to continue with new learning content. This module ensures students are equipped to proceed, maintaining the continuity and effectiveness of their learning.



**Fig. 1** Workflow of the Virtual Simulation System for 'Corneal Contact Lens' course

### Module 3 staged case selection module

Students can select cases from three difficulty levels (low, medium, high) based on their own assessment of their proficiency. After completing a case and its associated modules, they may choose to tackle a case from the next difficulty level. The system does not assess students' proficiency levels or progress between cases. However, it does provide a score for each case based on the students' performance in completing the case's tasks. Students are required to complete at least one case from each level, but the order in which they complete the levels is flexible. This approach allows them to solidify foundational knowledge while gradually tackling more complex cases.

### Module 4 case information display module

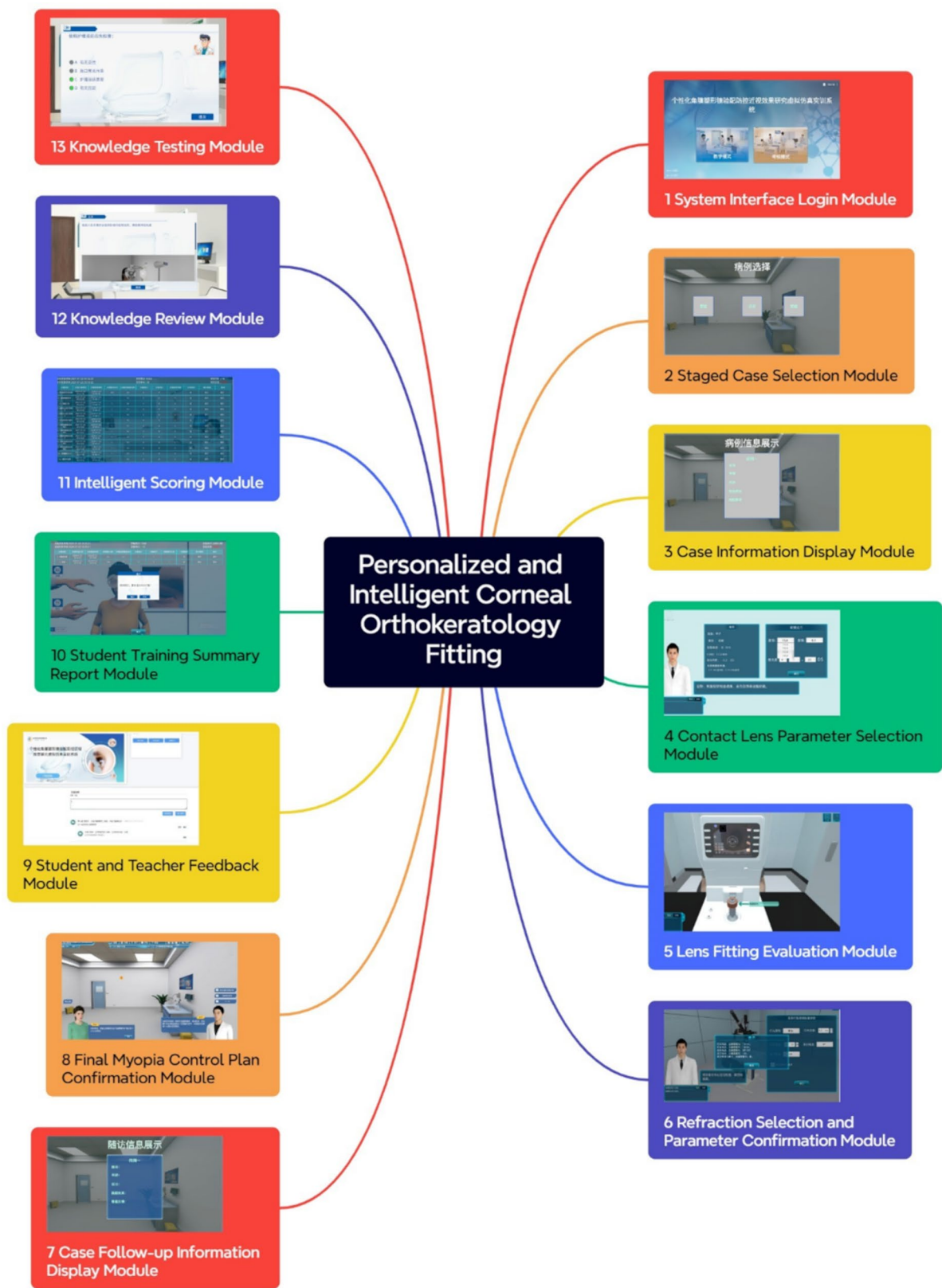
After selecting a case, the system displays detailed information about the case, including the patient's fitting needs and clinical background. Students are not required to complete all levels of difficulty before proceeding to the Case Information Display Module. They can choose the appropriate level of difficulty based on their learning progress and the system's recommendations. This comprehensive information allows students to understand the case fully, including symptoms, medical history, and fitting requirements, providing necessary background support for subsequent lens selection and parameter adjustments.

### Module 5 contact lens parameter selection module

In this module, students select appropriate contact lens trial parameters based on case information. They must consider detailed case specifics to choose the correct trial parameters, such as lens curvature and diameter. Through the use of VST, students can simulate real-life operations, enhancing their understanding and practical skills in parameter selection. The system intelligently integrates these parameters with an automated selection program, providing real-time feedback based on the students' choices, thereby helping them to compare their selected parameters with the system's intelligent recommendations.

### Module 6 lens fitting evaluation module

In this module, students evaluate the fit of the lenses, checking their suitability. Students who fail the Lens Fitting Evaluation Module are directed to the Lens Parameter Adjustment Module to modify the lens parameters and re-evaluate the fit. Students who pass the Lens Fitting Evaluation Module proceed directly to the next step without entering the adjustment module. The system uses a deep learning-based clinical fitting evaluation algorithm to compare the student's standard fit with the intelligent algorithm's assessment, providing timely feedback. This module helps students familiarize themselves



**Fig. 2** Application of the VST system in orthokeratology lens teaching 3 VST system evaluation

with and master evaluation methods, ensuring the lenses meet clinical requirements.

#### **Module 7 refraction selection and parameter confirmation module**

Upon passing the fitting evaluation, students enter the refraction selection and parameter confirmation module. Here, they select the appropriate refraction and confirm the final parameters based on the evaluation results and case information, ensuring the best corrective effect for the patient. The system provides guidance and confirmation processes for refraction selection, aiding in scientific decision-making.

#### **Module 8 case follow-up information display module**

The system displays follow-up information for the case, helping students understand the effects and subsequent handling of wearing corneal contact lenses. Students can see follow-up results, including the effectiveness of wearing the lenses and patient feedback, enhancing their understanding and handling of follow-up issues and improving their awareness and capability in patient care.

#### **Module 9 final myopia control plan confirmation module**

After reviewing follow-up information, students enter the final myopia control plan confirmation module to confirm the final myopia control plan and complete the case processing. They must integrate case information, trial lens evaluation results, refraction selection, and follow-up information to formulate and confirm the myopia control plan, simulating the actual clinical process of developing treatment plans and improving clinical decision-making skills.

#### **Module 10 student and teacher feedback module**

After completing the operations, the system provides evaluation functions for both students and teachers to assess and provide feedback on the entire operation process. This two-way feedback allows students to understand their performance and areas for improvement, and teachers to make instructional adjustments based on student feedback, enhancing interaction and communication and improving teaching quality.

#### **Module 11 student training summary report module**

The system generates a training summary report, recording students' learning progress and operational performance. The summary report details students' performance and achievements throughout the learning process, helping them understand their progress and providing targeted guidance and suggestions from teachers. This reflective process helps students consolidate knowledge and improve learning outcomes.

#### **Module 12 intelligent scoring module**

Based on students' operational performance, the system provides intelligent scoring. If the score is unsatisfactory, students need to return to the knowledge review module for further study. The intelligent scoring module ensures that students have mastered essential knowledge and skills, guiding them to targeted review and consolidation if needed, ensuring mastery of the relevant knowledge before proceeding.

#### **Module 13 knowledge review module**

In case of unsatisfactory scores, students return to the knowledge review module for further learning and consolidation. This module helps students re-learn and understand relevant knowledge points, offering diverse learning resources and exercises to effectively address knowledge and skill gaps.

#### **Questionnaire assessment**

This study conducted a longitudinal comparison of the course experience and self-learning ability of the same group of students from a university in Fujian Province before and after using the VST teaching system. The specific evaluation was carried out through questionnaires, including the Course Experience Questionnaire (CEQ) [9] and the Self-Directed Learning Ability Questionnaire [10]. Both questionnaires used a five-point rating scale. These two questionnaires can be found in [Supplementary Materials](#). The questionnaires were administered once at each of two points in time: first, before the implementation of the VST system, when students evaluated their experiences with traditional teaching methods used in the 'corneal contact lens' course, and second, after completing the course with the VST system. Informed consent was obtained from all participants, and the study was approved by the Biomedical Ethics Review Committee of Fujian Medical University.

Both the CEQ, developed by Ramsden and validated by Wilson et al. [9], and the SLAQ, adapted and validated by Shen et al. [10], have been previously validated in educational research. The internal consistency (Cronbach's alpha) of the CEQ exceeded 0.68 in samples of graduates from 1992 to 1994. For the SLAQ, the internal consistency (Cronbach's alpha) for the overall scale and its five dimensions in the pre-test administration were 0.799 (overall), 0.878, 0.843, 0.768, 0.768, and 0.800, respectively. In the post-test administration, the values were 0.862 (overall), 0.827, 0.806, 0.757, 0.770, and 0.772, respectively.

The CEQ assessed various aspects of the students' course experiences, such as the quality of teaching, the appropriateness of assessment methods, and the overall satisfaction with the course. The Self-Directed Learning Ability Questionnaire measured students' ability to take



**Table 1** Differences in course experience before and after using the virtual simulation system

Factor	Group	Mean	SD	Pvalue
Good Teaching Quality	Pre	4.05	0.39	< 0.0001
	Post	4.45	0.52	
Basic Skills	Pre	3.49	0.73	< 0.0001
	Post	4.40	0.56	
Clear Goals and Standards	Pre	3.49	0.78	< 0.0001
	Post	4.34	0.72	
Appropriate Learning Tasks	Pre	3.08	0.97	< 0.0001
	Post	4.26	0.86	
Suitable Evaluation Methods	Pre	3.05	1.07	< 0.0001
	Post	4.10	0.99	
Overall Course Experience Rating	Pre	3.07	1.05	< 0.0001
	Post	4.17	0.95	

initiative, set learning goals, and manage their learning processes independently.

### Outcome measures

The primary outcome measures in this study were two-fold. First, students' course experience was assessed using the CEQ, which evaluates various aspects of students' perceptions of their educational environment, including teaching quality, learning resources, and overall satisfaction. Second, self-directed learning abilities were measured using the SLAQ. This instrument assesses students' capacity for autonomous learning, including their ability to set learning goals, manage their time effectively, evaluate their progress, and apply appropriate learning strategies.

### Statistical analysis

In this study, GraphPad Prism 9 was used for statistical analysis. Descriptive statistical analysis was performed to understand students' acceptance and satisfaction with the virtual simulation laboratory teaching system. Considering that all the questionnaire scores do not follow a normal distribution, Wilcoxon Signed-Rank Test was employed to compare the differences in students' course experience and self-directed learning abilities before and after using the VST teaching system. Pearson correlation analysis was also conducted to determine the relationship between various factors of course experience and self-directed learning ability before and after the implementation of the system.

### Results

A total of 306 questionnaires were distributed (153 before using the VST system and 153 after using it), with 290 valid responses received. The survey respondents included 145 undergraduate optometry students, consisting of 71 males and 74 females, with an average age of  $21.05 \pm 0.82$  years.

**Table 2** Differences in self-directed learning ability before and after using the virtual simulation system

Factor	Group	Mean	SD	Pvalue
Expectations of Teacher's Role	Pre	3.91	0.63	< 0.0001
	Post	4.41	0.63	
Independence	Pre	3.03	0.93	< 0.0001
	Post	4.34	0.63	
Confidence in Learning Ability	Pre	3.02	0.90	< 0.0001
	Post	4.35	0.60	
Ability to Evaluate Learning Process	Pre	2.89	0.98	< 0.0001
	Post	4.33	0.69	
Use of Learning Strategies	Pre	3.37	0.81	< 0.0001
	Post	4.36	0.61	

### Course experience before and after using VST

There was a significant improvement in students' course experience before and after using the VST teaching system (Table 1). Specifically, students' evaluation of teaching improved from 4.05 to 4.45 after using VST, indicating that the introduction of VST enhanced students' recognition of teaching quality. Similarly, students' mastery of basic skills significantly increased, with scores rising from 3.49 to 4.40, demonstrating the effectiveness of VST in helping students grasp fundamental skills. Additionally, the clarity of course goals and standards improved, with scores increasing from 3.49 to 4.34, indicating that VST helps students better understand and achieve course objectives.

For the appropriateness of learning tasks, scores improved from 3.08 to 4.26, showing that VST made learning tasks more suitable for students' needs. In terms of the suitability of evaluation methods, scores rose from 3.05 to 4.10, reflecting that VST made evaluation methods more relevant to students' actual situations. The overall course experience score increased from 3.07 to 4.17, further demonstrating the positive impact of VST on students' overall learning experience.

### Self-directed learning ability before and after using VST

The use of the VST teaching system significantly enhanced students' self-directed learning abilities (Table 2). Specifically, before using the system, the average score for students' expectations of the teacher's role was 3.91 (SD=0.63), which increased to 4.41 (SD=0.63) after using it, indicating a significant increase in students' expectations of the teacher's role post-VST usage.

Additionally, students' independence scores increased significantly from an average of 3.03 (SD=0.93) before using the system to 4.34 (SD=0.63) after its use, showing a marked improvement in students' independence. Students' confidence in their learning ability also saw a significant increase, with average scores rising from 3.02 (SD=0.90) before using the system to 4.35 (SD=0.61)

after its use, demonstrating the VST system's positive impact on students' confidence.

Furthermore, the average score for students' ability to evaluate the learning process improved significantly from 2.89 (SD=0.98) before using the VST system to 4.33 (SD=0.69) after its use, indicating a notable enhancement in students' ability to assess their learning process. Finally, the average score for students' use of learning strategies increased from 3.37 (SD=0.81) before using the VST system to 4.36 (SD=0.61) after its use, suggesting that the VST system promoted the use of effective learning strategies among students.

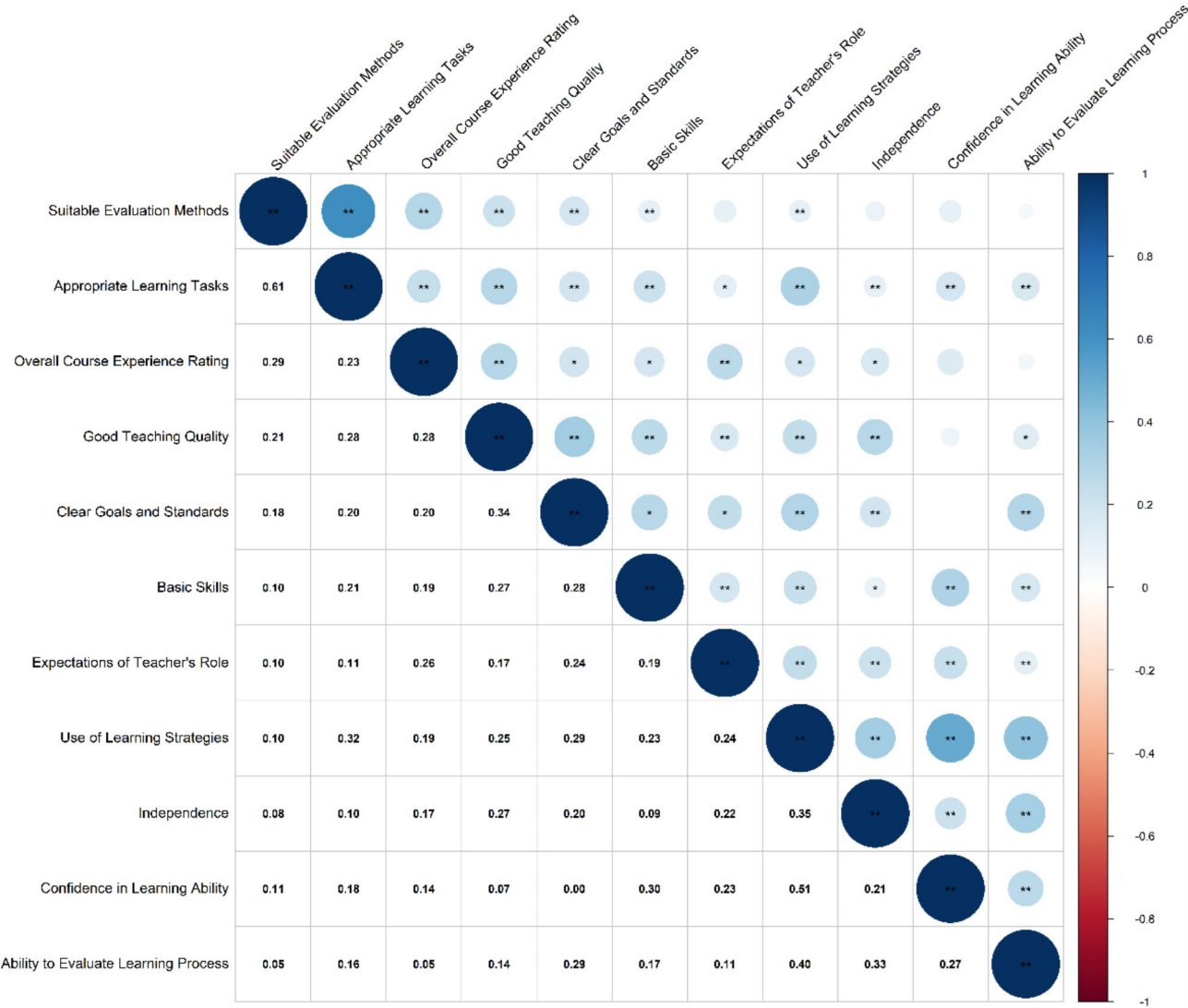
**Correlation analysis of factors related to course experience and self-directed learning ability before and after applying the VST teaching system**

As shown in Fig. 3, before using the VST teaching system, we found a high correlation between students' confidence in their learning ability and their ability to evaluate the learning process ( $r=0.78$ ). There was also a high correlation between the ability to evaluate the learning process and the use of learning strategies ( $r=0.73$ ), and between students' confidence in their learning ability and the use of learning strategies ( $r=0.76$ ).

However, as shown in Fig. 4, after using the VST teaching system, the correlations between these factors decreased. The correlation between students' confidence in their learning ability and their ability to evaluate the learning process was lower ( $r=0.27$ ). The correlation



**Fig. 3** Correlation Analysis Between Factors of Course Experience and Self-Directed Learning Ability Before the Application of the Virtual Simulation System. (\*indicates a  $p$ -value less than 0.05, \*\*indicate a  $p$ -value less than 0.01, \*\*\*indicate a  $p$ -value less than 0.001)



**Fig. 4** Correlation Analysis Between Factors of Course Experience and Self-Directed Learning Ability After the Application of the Virtual Simulation System. (\*indicates a *p*-value less than 0.05, \*\*indicate a *p*-value less than 0.01, \*\*\*indicate a *p*-value less than 0.001)

between the use of learning strategies and the ability to evaluate the learning process was also lower ( $r=0.40$ ), and the correlation between the use of learning strategies and students' confidence in their learning ability was reduced ( $r=0.51$ ).

Discussion

Recently, the use of corneal contact lenses has significantly increased, becoming important tools for vision correction and eye care [11]. With technological advancements, the types and materials of contact lenses have continuously improved, offering better comfort and breathability for various vision problems such as myopia, hyperopia, astigmatism, and presbyopia [12, 13]. Additionally, the use of corneal contact lenses for cosmetic purposes and special applications (such as sports

and specific professions) has become increasingly popular [14]. Wearing contact lenses inevitably leads to ocular changes and may cause contact lens-related diseases such as corneal neovascularization and microbial keratitis [15, 16]. Therefore, proper lens wear, lens care, and follow-up are crucial for the long-term safe use of corneal contact lenses [17]. Moreover, proper fitting education, fitting equipment, and necessary professional standards are fundamental requirements for initiating orthokeratology lens fitting [18]. VST has demonstrated potential in educational training for burn care, chemotherapy, surgery, and dentistry [19, 20]. However, its application in the teaching of 'corneal contact lens' courses remains relatively limited. In traditional courses, students primarily learn through lectures and textbook readings with limited clinical exposure. VST offers a more immersive,



hands-on learning experience that compensates for the lack of patient interaction in conventional teaching. To better utilize VST in teaching, subtly engaging students and enhancing fitting skills, this study developed and applied a virtual simulation teaching system for 'corneal contact lens'. Through questionnaires, we collected data on students' course experience and self-directed learning ability with this system. Correlation analysis was performed to investigate the relationships between various factors of students' course experience and self-directed learning ability, both before and after using the VST system. This analysis aimed to assess how the introduction of virtual simulation technology affected these interrelated factors.

This study showed that students' course experience significantly improved after using the system. Students' recognition of teaching quality and understanding of course objectives notably increased. This indicates that the introduction of VST made the teaching content more vivid and intuitive, enhancing students' engagement. Ma et al. [21] also found that virtual simulation learning environments can improve the quality of physiology education by promoting active learning, and visualizing physiological processes. Singh et al. [22] found that virtual simulation environments had a significant positive impact on students' knowledge, learning motivation, and cognition in electronic experimental courses. Additionally, VST simulates real operating environments, enabling students to practice virtually, thereby reducing reliance on physical experimental conditions and enhancing both the frequency and effectiveness of contact lens fitting practice. This aligns with Bekelis et al. [23], who proposed that immersive preoperative virtual simulation experiences could enhance satisfaction during surgery and minimize stress, thereby improving the perioperative experience.

Furthermore, the use of the VST teaching system significantly improved students' self-directed learning abilities in 'corneal contact lens' course ( $P < 0.0001$ ). After using the system, students' expectations of the teacher's role, independence, confidence in learning ability, ability to evaluate the learning process, and use of learning strategies all showed significant improvement. This suggests that VST not only provides rich learning resources and a platform for self-directed learning but also, through intelligent feedback and evaluation systems, helps students better track their learning progress and outcomes, enhancing their self-directed learning abilities and confidence. George et al. [24] also found that the environments with VST could improve learning outcomes, promote self-directed learning, achieve multisensory learning, enhance spatial ability, confidence, and enjoyment, and reduce cognitive load. Abdullah et al. [25] supported this view, finding that using virtual simulation in problem-based learning could enhance students' group

collaboration skills and self-directed learning abilities. While mastering professional knowledge, students can also engage in innovative development and application based on virtual simulation technology, contributing to teaching. Morales et al. [26] also found that project-based learning in virtual simulation classrooms was very effective for high school students, promoting independent learning and peer-guided learning even with minimal teacher guidance.

Finally, to observe the correlation between students' course experience and self-directed learning abilities, we conducted a Pearson correlation analysis. Previous studies have suggested that Pearson correlation coefficients of  $< 0.4$ ,  $0.4-0.7$ , and  $> 0.7$  indicate low, medium, and high correlations, respectively [27]. Our study found significant positive correlations between the use of learning strategies, students' confidence in their learning abilities, and their ability to evaluate the learning process before using the virtual simulation teaching system. This indicates that in traditional teaching models, students' confidence in their learning abilities and their ability to evaluate the learning process relied on the use of learning strategies. Learning strategies in this study refer to the methods students used to guide their learning, such as goal-setting, self-monitoring, and utilizing feedback. After using the virtual simulation system, the correlation between these strategies and students' confidence in their learning abilities decreased, suggesting that the system itself provided enough guidance to reduce reliance on these strategies, promoting a more independent learning process. The virtual simulation teaching system, by providing a more realistic practice environment and interactive experience, fostered the development of students' practical skills and problem-solving abilities, thereby enhancing overall learning outcomes.

Despite the significant effects of VST on the teaching of 'corneal contact lens' courses demonstrated in this study, there are still some limitations. First, a major limitation of this study is the lack of a control group. Future studies should include a control group that does not use the virtual simulation technology to better evaluate the impact of the VST on learning outcomes. Second, the sample size was relatively small, limited to a group of students from a university in Fujian Province of China, so the generalizability of the results needs further verification. Third, this study mainly relied on questionnaires, and although standardized scales were used, there might be some bias in students' subjective evaluations. Future studies could expand the sample size and use more objective assessment indicators, such as practical skills tests and clinical internship performance, to further validate the application effects of VST technology in corneal contact lens course teaching.

Future research can explore the application of VST in other medical education fields, such as ophthalmic surgery training and optometric diagnostic techniques. By collaborating with multiple hospital, continuously upgrading and supplementing the case database, and promoting the teaching model towards autonomous experience enhancement. An open teaching framework that focuses on the characteristics of optometry professional training and sets up open myopia control extension modules can be adopted to create an immersive new classroom supporting self-exploration and collaborative learning and provide valuable references for the teaching reform of optometry.

## Conclusion

The application of virtual simulation technology in teaching a corneal contact lens course can significantly enhance students' course experience and independent learning. Guided by the new medical education concepts and oriented towards the responsibilities and social awareness of optometrists in myopia control, this approach emphasizes enhancing students' orthokeratology fitting skills and their awareness of myopia prevention. Through these experiments, students not only mastered operational techniques but also applied theoretical knowledge to practical operations, deepening their understanding and retention of optometric principles.

This study provides new insights and practical evidence for the application of virtual simulation technology in optometry education. By establishing a highly challenging "Virtual Simulation Experimental Teaching 2.0" training platform, it provides the strategies for eye health and myopia prevention, accelerating the cultivation of high-quality professionals urgently needed in the field of myopia control.

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12909-024-06378-y>.

Supplementary Material 1

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## Author contributions

LL: Experimental design, manuscript writing; KX: Data statistical analysis, and chart creation; JL: Guidance on intelligent technology; HM, SL, XL, JW, QC: Questionnaire collection and organization; YH: Research guidance, manuscript review, and funding support.

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## Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

## Declarations

### Ethics approval and consent to participate

This study was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki. All participants provided written informed consent prior to their participation in the study. Participation was voluntary, and respondents were assured of the confidentiality and anonymity of their responses. The study ensured that no personally identifiable information was collected or disclosed during the course of the research. Our study was submitted to the Biomedical Ethics Review Committee of Fujian Medical University and was approved accordingly.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

### Clinical trial number

Not applicable.

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