

Submission ID #: 71182

Scriptwriter Name: Sri Lakshmi Priya

Project Page Link: <https://review.jove.com/account/file-uploader?src=21710558>

Title: A Study on an Intelligent Diagnosis and Treatment Assistant System for Acupuncture in Diminished Ovarian Reserve Based on a Knowledge Graph

Authors and Affiliations:

Zijing Zhu^{1,2}, Junchen Lu^{1,2}, Kefan Li^{1,2}, Jing Wen¹, Yueying Huang¹, Zhiyuan LV^{1,2}, Chen Li³, Youbing Xia^{1,2}, Tiancheng Xu^{1,2}

¹Key Laboratory of Acupuncture and Medicine Research of Ministry of Education, Nanjing University of Chinese Medicine

²School of Medical Information and Engineering, Xuzhou Medical University

³Department of Reproductive Medicine, Affiliated Jinling Hospital, Medicine School of Nanjing University

Corresponding Authors:

Youbing Xia	xybd1968@njucm.edu.cn
Tiancheng Xu	xtc@njucm.edu.cn

Email Addresses for All Authors:

Zijing Zhu	yetiecho@163.com
Junchen Lu	19930723246@163.com
Kefan Li	981554584@qq.com
Jing Wen	wwenjingmail@163.com
Yueying HUANG	20210475@njucm.edu.cn
Zhiyuan LV	zylv0702@163.com
Chen Li	chenli1978@nju.edu.cn
Youbing Xia	xybd1968@njucm.edu.cn
Tiancheng Xu	xtc@njucm.edu.cn

Author Questionnaire

1. Microscopy: Does your protocol require the use of a dissecting or stereomicroscope for performing a complex dissection, microinjection technique, or something similar? **No**

2. Software: Does the part of your protocol being filmed include step-by-step descriptions of software usage? **Yes**

3. Filming location: Will the filming need to take place in multiple locations? **NO**

4. Testimonials (optional): Would you be open to filming two short testimonial statements **live during your JoVE shoot**? These will **not appear in your JoVE video** but may be used in JoVE's promotional materials. **YES**

If **Yes**, please provide the **full name and position** (e.g., Director of [Institute Name], Senior Researcher [University Name], etc.) of the author willing to participate.

Zijing Zhu, PhD Candidate

Current Protocol Length

Number of Steps: 17

Number of Shots: 51

Interviews

Videographer: Obtain headshots for all authors available at the filming location.

INTRODUCTION:

~~REQUIRED: Summarize your research focus and the main questions it aims to answer.~~

- 1.1. **Zijing Zhu:** Our research focuses on developing an intelligent acupuncture system for Diminished Ovarian Reserve diagnosis and treatment.
 - 1.1.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera.

~~Describe the research contexts or systems in which this protocol can be applied.~~

- 1.2. **Zijing Zhu:** This protocol can be applied to acupuncture research involving Diminished Ovarian Reserve and other gynecologic reproductive diseases.
 - 1.2.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera.

CONCLUSION:

~~What does this protocol allow researchers to study or measure?~~

- 1.3. **Zijing Zhu:** This approach enables researchers to assess diagnostic agreement and acupuncture prescription appropriateness.
 - 1.3.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera.

~~Are there any additional methods or analyses that can be performed following this procedure?~~

- 1.4. **Zijing Zhu:** Researchers can additionally perform LLM-based reasoning analysis, multi-center validation, and long-term efficacy follow-up using this procedure.
 - 1.4.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera.

~~How can future studies build on this work? Describe the questions or research directions that can be investigated next.~~

- 1.5. **Zijing Zhu:** Future studies can build on this work by expanding applications to additional diseases, integrating multimodal data, and conducting prospective studies.
 - 1.5.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera.

Videographer: Obtain headshots for all authors available at the filming location.

Testimonial Questions (OPTIONAL):

Videographer: Please capture all testimonial shots in a wide-angle format with sufficient headspace, as the final videos will be rendered in a 1:1 aspect ratio. Testimonial statements will be presented live by the authors, sharing their spontaneous perspectives.

- Testimonial statements will **not appear in the video** but may be featured in the journal's promotional materials.
- **Provide the full name and position** (e.g., Director of [Institute Name], Senior Researcher [University Name], etc.) of the author delivering the testimonial.
- Please **answer the testimonial question live during the shoot**, speaking naturally and in your own words in **complete sentences**.

~~What value do you expect this video/article to have for other researchers working in your field?~~

1.6. **Zijing Zhu, PhD Candidate:** (authors will present their testimonial statements live)

1.6.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

~~How does the video format of your article help you to share your work with the broader scientific community?~~

1.7. **Zijing Zhu, PhD Candidate:** (authors will present their testimonial statements live)

1.7.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

Ethics Title Card

This research has been approved by the Ethics Committee at the General Hospital of the Eastern Theater Command

Protocol

***Videographer:** Please always record an audio slate while filming each shot mentioned in the shotlist.*

NOTE: SCREEN timestamps for protocol were added at the postshoot stage. Please contact the postshoot note integrator (Sri Lakshmi Priya) for queries regarding lab media.

2. Construction of Knowledge graph

Demonstrator: Zijong Zhu

2.1. To begin, collect data from classical acupuncture texts, Chinese-language literature from the China National Knowledge Infrastructure or CNKI (*C-N-K-I*), clinical data from reproductive centers at tertiary hospitals [1], English-language literature from the Web of Science Core Collection, and standardized knowledge bases through trained personnel [2].

2.1.1. WIDE: Talent seated at a large workstation with books, printed journal articles, and computer monitors. Videographer and Author's NOTE: Due to the unavailability of a large workstation, this shot was filmed in a regular office environment

2.1.2. SCREEN: 71182_screenshot_1.mp4: 00:00-00:16

2.2. Perform data annotation and select data according to the inclusion and exclusion criteria [1]. Include 400 clinical cases to support the identification of diagnostic and therapeutic patterns [2].

2.2.1. SCREEN: 71182_screenshot_2.mp4: 00:00-00:09

2.2.2. SCREEN: 71182_screenshot_3.mp4: 00:00-00:10

2.3. Using a standardized annotation platform, manually annotate approximately 30 percent of the data, including classical texts and semantically complex content [1]. With large language models or LLMs (*L-L-M-S*), process 70 percent of the data for entity recognition, relationship extraction, and terminology normalization [2]. Review the generated results [3].

2.3.1. SCREEN: 71182_screenshot_4.mp4: 00:00-00:10

2.3.2. SCREEN: 71182_screenshot_5.mp4: 00:00-00:15

2.3.3. SCREEN: 71182_screenshot_6.mp4: 00:00-00:07

2.4. Using structured prompt templates designed to guide LLM, perform automated extraction [1]. Once the model role is defined as a domain-specific knowledge

extraction expert, include a few-shot learning example in JavaScript Object Notation or JSON (*J-Son*) triplet format to improve extraction performance [2].

2.4.1. SCREEN: 71182_screenshot_7.mp4: 00:00-00:08

2.4.2. SCREEN: 71182_screenshot_8.mp4: 00:01-00:08

2.5. Using JSON validation tools, serialize validated knowledge triplets into independent JSON files named according to their source documents to maintain traceability [1].

2.5.1. SCREEN: 71182_screenshot_9.mp4: 00:00-00:06

2.6. Store the finalized knowledge graph in a graph database using Python-based frameworks [1]. Visualize the knowledge graph using built-in graph database tools to support inspection and validation [2].

2.6.1. SCREEN: 71182_screenshot_10.mp4: 00:00-00:12

2.6.2. SCREEN: 71182_screenshot_11.mp4: 00:00-00:14

3. Development of Application System

3.1. Develop the application system based on the constructed knowledge graph to enable clinical decision support [1] and process user input data accordingly [2].

3.1.1. SCREEN: 71182_screenshot_12.mp4: 00:00-00:12.

3.1.2. SCREEN: 71182_screenshot_13.mp4: 00:00-00:09.

3.2. Using the bidirectional long short-term memory conditional random field or BiLSTM-CRF (*Bye-L-S-T-M-C-R-F*) model, implement natural language understanding for named entity recognition and entity linking [1].

3.2.1. SCREEN: 71182_screenshot_14.mp4: 00:00-00:09

3.3. Build the model architecture with an embedding layer trained on domain-specific corpora [1], a bidirectional long short-term memory layer to capture contextual information [2], and a conditional random field layer to ensure optimal sequence labeling [3].

3.3.1. SCREEN: 71182_screenshot_15.mp4: 00:00-00:08

3.3.2. SCREEN: 71182_screenshot_16.mp4: 00:00-00:09

3.3.3. SCREEN: 71182_screenshot_17.mp4: 00:00-00:09

3.4. Train the model on manually annotated clinical and literature data, with annotations performed independently by domain experts [1]. Using Cohen's kappa coefficient, assess inter-annotator agreement with a threshold of at least 0.85 and resolve discrepancies through expert consensus [2].

3.4.1. SCREEN: 71182_screenshot_18.mp4: 00:00-00:08

3.4.2. SCREEN: 71182_screenshot_19.mp4: 00:00-00:10

- 3.5. During inference, extract structured entities, including symptoms, diseases, and syndrome patterns, from clinical input data [1]. Map these entities to standardized nodes in the knowledge graph [2].
 - 3.5.1. SCREEN: 71182_screenshot_20.mp4: 00:00-00:06
 - 3.5.2. SCREEN: 71182_screenshot_21.mp4: 00:00-00:07
- 3.6. Using a dual-mode strategy, perform knowledge retrieval combining keyword-based and semantic-based approaches [1]. Use vector representations to identify relevant unstructured knowledge [2].
 - 3.6.1. SCREEN: 71182_screenshot_22.mp4: 00:00-00:08
 - 3.6.2. SCREEN: 71182_screenshot_23.mp4: 00:00-00:08
- 3.7. Merge keyword-based and semantic-based retrieved results [1]. Identify and remove duplicates, and structure results for downstream processing [2]. Adjust weights for gynecological and diminished ovarian reserve-related contexts [3].
 - 3.7.1. SCREEN: 71182_screenshot_24.mp4: 00:00-00:07
 - 3.7.2. SCREEN: 71182_screenshot_25.mp4: 00:00-00:05
 - 3.7.3. SCREEN: 71182_screenshot_26.mp4: 00:00-00:05
- 3.8. Using natural language generation techniques, generate diagnostic and treatment outputs and convert structured knowledge into clinically interpretable responses [1].
 - 3.8.1. SCREEN: 71182_screenshot_27.mp4: 00:00-00:09

4. Clinical Application and Evaluation

- 4.1. After applying the developed system in a clinical setting, recruit participants diagnosed with diminished ovarian reserve according to the inclusion and exclusion criteria [1].
 - 4.1.1. Patients with diminished ovarian reserve reviewing and signing consent forms.
- 4.2. Collect and record patient demographic and clinical information in a structured format [1]. Generate diagnostic outputs and acupuncture prescriptions based on the input data [2].
 - 4.2.1. SCREEN: 71182_screenshot_28.mp4: 00:00-00:09
 - 4.2.2. SCREEN: 71182_screenshot_29.mp4: 00:00-00:09
- 4.3. Once the system performance is evaluated using diagnostic accuracy and treatment appropriateness, compare system-generated syndrome differentiation results with results provided by 3 senior gynecological Traditional Chinese Medicine physicians serving as the reference standard [1]. Calculate the diagnostic agreement rate as the proportion of consistent cases among all cases [2].
 - 4.3.1. SCREEN: 71182_screenshot_30.mp4: 00:00-00:10
 - 4.3.2. SCREEN: 71182_screenshot_31.mp4: 00:00-00:07

- 4.4. Evaluate treatment appropriateness using a panel of 3 senior acupuncturists with at least 5 years of clinical experience and senior professional titles, and have experts independently assess system-generated prescriptions using a 5-point Likert scale [1]. Evaluate inter-rater agreement using Kendall's coefficient of concordance [2].
 - 4.4.1. SCREEN: 71182_screenshot_32.mp4: 00:00-00:08
 - 4.4.2. SCREEN: 71182_screenshot_33.mp4: 00:00-00:09

Results

5. Results

- 5.1. A total of 374 Chinese-language sources [1], 267 English-language articles [2], and 82 classical traditional Chinese medicine texts were incorporated into the knowledge graph [3].
 - 5.1.1. LAB MEDIA: Figure 5. *Video editor: Emphasize the blue segment labelled as Chinese literature.*
 - 5.1.2. LAB MEDIA: Figure 5. *Video editor: Emphasize the orange segment labelled as English articles.*
 - 5.1.3. LAB MEDIA: Figure 5. *Video editor: Emphasize the yellow segment labelled as TCM books.*
- 5.2. The full knowledge graph contained 16558 entities across 7 predefined categories [1] and 80084 relations spanning 21 relation types [2].
 - 5.2.1. LAB MEDIA: Table 1. *Video editor: Emphasize the value 16558 under entities in full knowledge graph row.*
 - 5.2.2. LAB MEDIA: Table 1. *Video editor: Emphasize the value 80084 under relations in full knowledge graph row.*
- 5.3. Among 90 patients, age ranged from 22 to 54 years [1], with a peak at 32 years [2] and the highest concentration in the 31 to 35-year age group [3].
 - 5.3.1. LAB MEDIA: Figure 10.
 - 5.3.2. LAB MEDIA: Figure 10. *Video editor: Emphasize the bar at 32 years*
 - 5.3.3. LAB MEDIA: Figure 10. *Video editor: Emphasize the bars in the 31–35-year age group*
- 5.4. Self-Rating Anxiety Scale assessment showed that 57% of patients had normal scores [1], 28% had subclinical anxiety levels [2], and smaller proportions had mild, moderate, or severe anxiety [3].
 - 5.4.1. LAB MEDIA: Figure 11. *Video editor: Emphasize the blue segment with 57% labelled as <40.*
 - 5.4.2. LAB MEDIA: Figure 11. *Video editor: Emphasize the orange segment with 28% labelled as 40-49.*
 - 5.4.3. LAB MEDIA: Figure 11. *Video editor: Emphasize the yellow, green and teal coloured segments labelled as 50-59, 60-69 and >70.*
- 5.5. Diagnostic agreement between system-generated outputs and expert clinician assessments was 86.7% [1].

- 5.5.1. LAB MEDIA: Table 2. Video editor: *Emphasize the value 86.7 under diagnostic agreement rate.*
- 5.6. Treatment appropriateness had a mean score of 4.65 on a 5-point Likert scale [1].
- 5.6.1. LAB MEDIA: Table 3. *Video editor: Emphasize the value 4.65 under average score.*
- 5.7. Inter-rater agreement among expert evaluators measured using Kendall's coefficient of concordance, was approximately 0.13 [1], suggesting a statistically significant level of agreement, although the overall concordance remained limited [2].
- 5.7.1. LAB MEDIA: Table 3. *Video editor: Emphasize the value 0.13 under Kendall's W.*
- 5.7.2. LAB MEDIA: Table 3.

Pronunciation guides:

1. Acupuncture
Pronunciation link: <https://www.merriam-webster.com/dictionary/acupuncture>
IPA: /'æk.jə.pʌŋk.tʃə/
Phonetic Spelling: ak-yuh-pungk-cher
2. Reproductive
Pronunciation link: <https://www.merriam-webster.com/dictionary/reproductive>
IPA: /,ri:.prə'dʌk.tɪv/
Phonetic Spelling: ree-pruh-duhk-tiv
3. Annotation
Pronunciation link: <https://www.merriam-webster.com/dictionary/annotation>
IPA: /,æn.ə'teɪ.ʃən/
Phonetic Spelling: an-uh-tay-shuhn
4. Semantic
Pronunciation link: <https://www.merriam-webster.com/dictionary/semantic>
IPA: /sə'mæn.tɪk/
Phonetic Spelling: suh-man-tik
5. Entity
Pronunciation link: <https://www.merriam-webster.com/dictionary/entity>
IPA: /'en.tə.ti/
Phonetic Spelling: en-tuh-tee
6. Terminology
Pronunciation link: <https://www.merriam-webster.com/dictionary/terminology>
IPA: /,tɜ:.mə'nɑ:.lə.dʒi/
Phonetic Spelling: tur-muh-nol-uh-jee
7. Extraction
Pronunciation link: <https://www.merriam-webster.com/dictionary/extraction>

IPA: /ɪk'stræk.jən/

Phonetic Spelling: ik-strak-shuhn

8. JavaScript

Pronunciation link: <https://www.merriam-webster.com/dictionary/JavaScript>

IPA: /'dʒɑː.və.skɹɪpt/

Phonetic Spelling: jah-vuh-skript

9. Notation

Pronunciation link: <https://www.merriam-webster.com/dictionary/notation>

IPA: /noʊ'teɪ.jən/

Phonetic Spelling: noh-tay-shuhn

10. Serialize

Pronunciation link: <https://www.merriam-webster.com/dictionary/serialize>

IPA: /'sɪr.i.ə.laɪz/

Phonetic Spelling: seer-ee-uh-lyze

11. Traceability

Pronunciation link: <https://www.merriam-webster.com/dictionary/traceability>

IPA: /ˌtreɪ.sə'bɪl.ə.ti/

Phonetic Spelling: tray-suh-bil-uh-tee

12. Knowledge

Pronunciation link: <https://www.merriam-webster.com/dictionary/knowledge>

IPA: /'nɑː.lɪdʒ/

Phonetic Spelling: nol-ij

13. Database

Pronunciation link: <https://www.merriam-webster.com/dictionary/database>

IPA: /'deɪ.tə.beɪs/, /'dæt.ə.beɪs/

Phonetic Spelling: day-tuh-base; dat-uh-base

14. Bidirectional

Pronunciation link: <https://www.merriam-webster.com/dictionary/bidirectional>

IPA: /ˌbaɪ.də'rek.jənəl/, /ˌbaɪ.də'rek.jənəl/

Phonetic Spelling: bye-duh-rek-shuh-nuhl

15. Contextual

Pronunciation link: <https://www.merriam-webster.com/dictionary/contextual>

IPA: /kən'teks.tʃu.əl/

Phonetic Spelling: kuhn-teks-choo-uhl

16. Inter-annotator

Pronunciation link: <https://www.merriam-webster.com/dictionary/annotator>

IPA: /'æn.ə.teɪ.tə/

Phonetic Spelling: an-uh-tay-ter

17. Inference

Pronunciation link: <https://www.merriam-webster.com/dictionary/inference>

IPA: /'ɪn.fə.əns/

Phonetic Spelling: in-fer-uhns

18. Gynecological
Pronunciation link: <https://www.merriam-webster.com/dictionary/gynecological>
IPA: /ˌɡaɪ.nə.kəˈlɑː.dʒɪ.kəl/
Phonetic Spelling: guy·nuh·kuh·loj·i·kuhl
19. Ovarian
Pronunciation link: <https://www.merriam-webster.com/dictionary/ovarian>
IPA: /oʊˈver.i.ən/
Phonetic Spelling: oh·vair·ee·uhn
20. Acupuncturists
Pronunciation link: <https://www.merriam-webster.com/dictionary/acupuncturist>
IPA: /ˈæk.jə.pʌŋk.tʃə.ɪst/
Phonetic Spelling: ak·yuh·pungk·cher·ist
21. Concordance
Pronunciation link: <https://www.merriam-webster.com/dictionary/concordance>
IPA: /kənˈkɔːr.dəns/
Phonetic Spelling: kuhn·kor·duhns
22. Likert
Pronunciation link: <https://www.merriam-webster.com/dictionary/Likert%20scale>
IPA: /ˈlɪk.ət/
Phonetic Spelling: lik·ert
23. Diagnostic
Pronunciation link: <https://www.merriam-webster.com/dictionary/diagnostic>
IPA: /ˌdaɪ.əɡˈnɔː.stɪk/
Phonetic Spelling: dye·ug·nos·tik
24. Demographic
Pronunciation link: <https://www.merriam-webster.com/dictionary/demographic>
IPA: /ˌdem.əˈɡræf.ɪk/
Phonetic Spelling: dem·uh·graf·ik
25. Traditional
Pronunciation link: <https://www.merriam-webster.com/dictionary/traditional>
IPA: /trəˈdɪʃ.ə.nəl/
Phonetic Spelling: truh·dish·uh·nuhl