

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:

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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.

Please inform Swati Madhu and Sri Lakshmi Priya once the rough video is ready, as the English translation needs to be added.

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.jən/
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.skript/

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