Searching for Clinical Evidence in CiteSpace

Chaomei Chen, Yunan Chen
College of Information Science and Technology, Drexel University, Philadelphia, PA
Email: chaomei.chen@cis.drexel.edu, yc337@drexel.edu

Abstract. A crucial step in the practice of evidence-based medicine is to locate the best available evidence regarding to clinical questions. In this article, we demonstrate that combining visualization techniques with traditional methods developed in evidence-based medicine could simplify the task. We describe a unifying framework for searching clinical evidence across multiple sources such as highly cited articles in the Web of Science and articles of particular types of study design in PubMed. We describe the implementation of a prototyping system to visualize the distribution of available evidence in a broader context of the underlying subject domain. We include examples of evidence found in the heart diseases and lung cancer literature. Practical implications on the design of visualization-based evidence searching tools are discussed.

INTRODUCTION

Evidence-based medicine (EBM) is a paradigm in medicine that emphasizes the essential role of scientifically found evidence in making clinical decisions and training [1]. The most notable types of evidence are randomized controlled trials (RCTs), systematic reviews (SRs), and meta-analyses. The practice of EBM consists of 5 steps [2, 3]:

1. Identify clinical questions,
2. Search for the best external evidence,
3. Clinically appraise the validity and importance of the evidence,
4. Put it into clinical practice, and
5. Evaluate the performance.

In this article, we focus on the second step, i.e. searching for the best evidence. Searching for the best evidence is a critical component of EBM. We propose an integrative approach that could potentially compliment conventional search methods with a reduced complexity and reduced costs. The new method is designed to enable users to retrieve the best available evidence in a broader context of the subject domain.

We are particularly interested in the potential role of highly cited publications of studies as proxies of best evidence so that searching for best evidence can be improved in terms of efficiency. Knowledge domain visualization techniques are used to detect and depict emerging trends and interrelationships between research front terms and highly cited articles. The most common types of evidence are shown in visualized associative networks in such a way that one can easily access how they are related to other articles and when significant connections are made.

BACKGROUND

The strength of clinical evidence has been conceptualized in a number of hierarchical systems. For example, Oxford Centre for Evidence-Based Medicine classifies evidence into five levels, from the strongest evidence at level 1 to the weakest at level 5. In particular, SRs with homogeneity of RCTs are top-level evidence (level 1a). Individual RCTs with a narrow confidence interval are the second best (level 1b). National Cancer Institute [4] defines levels of evidence for cancer treatments based on a simpler system. Randomized, double-blinded controlled clinical trials are regarded as the gold standard because it provides protection from allocation bias by the investigator and from bias in assessment of outcomes by both the investigator and the patient. However, it does not give meta-analysis a higher status than randomized studies because of various known weaknesses of meta-analysis [5, 6].

An authoritative source of evidence is the systematic reviews prepared and maintained by the Cochrane Collaboration [7, 8]. Cochrane reviews' reputation is partly drawn from their regular updates and revisions. Medline, through its web-based interface PubMed, is probably the most widely used source of evidence. A Medline record contains a publication type field to index the type of study design, including *randomized controlled clinical trial*, *clinical trial*, and *meta-analysis*. The provision of the publication type [pt] makes it possible to search for RCTs related to a given topic.

In a recent example, the publication type in Medline records was used to search for meta-analysis, RCTs, and simple MeSH term matches to given clinical questions [3]. The grades of recommendations and levels of evidence were determined by following the first three steps of the EBM procedure regarding the topic of general thoracic surgery. They followed the strategy described in [9] by searching for meta-analysis in the publication type field. Similarly, the publication type was also used for searching for RCTs.

A potentially desirable piece of information missing in Medline records is how frequently an article has been cited by other publications. The times of citation can provide informative insights into the popularity of an article. High-quality publications, among several other types, tend to be highly cited. Such additional information may help EBM practitioners in their evidence searching tasks and could even play a role in subsequent critical appraisals because it is an indicator of consensus in medical research.

The widely known source of scientific citations is the Science Citation Index (SCI) maintained by the Institute for Scientific Information (ISI). An ISI's bibliographic record contains a field called Cited References (CR). The number of times a given article has been cited can be derived from such lists. In fact, the number of citations within the entire citation databases is stored in a Times Cited (TC) field. Citation analysis has a long history in information science. Co-citations are instances in which two articles are referenced together in subsequently published articles. Using co-citation relationships as a grouping mechanism to identify latent structures in scientific literature is a particularly vibrant area of research [10, 11].

CiteSpace is a series of design, implementation, and refinement efforts [12-15]. Its primary goal is to provide a wide range of users a visual exploration tool so as to identify emerging trends and transient patterns in scientific literature. CiteSpace visualizes interrelationships between scientific articles based on their co-citation patterns. Emerging trends and thematic transitions are visualized in terms of how topical terms with a sharply increased frequency change over time. We used CiteSpace in a number of domain visualization studies of paradigm shift and abrupt changes, including the superstring revolutions in physics, the mass extinction debates, and emerging trends in research of terrorist events such as the Oklahoma City bombing and the September 11, 2001 attacks. However, we have not applied the approach to EBM, in particular, to support the evidence search task. To our knowledge, we are not aware of visual exploration tools designed for searching specific types of evidence in the context of their home domain. We propose a conceptual framework to extend the knowledge domain visualization techniques to support evidence search tasks in EBM.

CONCEPTUAL FRAMEWORK

The conceptual framework is based on the simple assumption that combining multiple mutually complement sources of evidence can improve the search quality and efficiency. This is akin to search in a meta-search engine, but with additional visual exploration supports. In this article, we focus on PubMed and the Web of Science. As shown in Figure 1, the framework can be extended to incorporate additional sources.

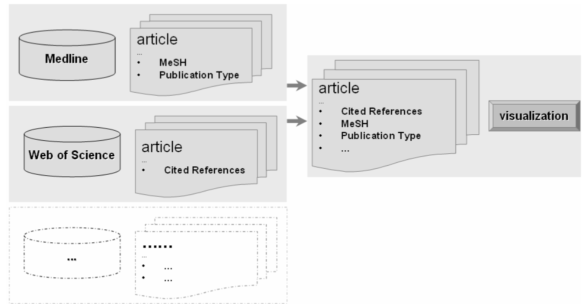

Figure 1. A unifying framework for finding evidence across complementary sources. Clinical evidence in subsequent visualizations is marked by publication type.

A practical issue is that although PubMed is openly accessible, the Web of Science is subscription-based and making a local copy of any of them is impractical. As the first step towards supporting EBM, we design and implement the following method to easy this problem. Suppose our aim is to locate the best evidence regarding lung cancer treatments. The procedure is as follows:

1. Search for articles in the Web of Science on lung cancer (the search is intentionally broad).
2. Visualize the search results in CiteSpace, including emerging trends and temporal patterns.
3. Automatically annotated articles with specified publication types, namely meta-analysis, randomized controlled clinical trial, and clinical trial.
4. Explore the visualization map and select articles for critical appraisals.
5. (Repeat the procedure periodically or as needed).

In our current implementation, an efficient annotation of visualizations is automated by retrieving the publication type information from PubMed real-time through multiple concurrently running Java threads. The process is transparent and non-intrusive to the user. It is integrated smoothly with the normal visualization process. The only way the user can tell the behind-the-scene search is when an increasing number of articles are annotated with publication types. The additional search is cost-effective and efficient, and the user does not even need to cache the information locally.

We expect to identify unique features associated with the best evidence in the visualizations of associative networks of articles and topic terms. Will we find the best evidence at hubs of clusters or bridges between clusters? In the new automatically annotated visualization, the publication type of three types of EBM evidence are marked as '**r**' for randomized controlled clinical trial, '**c**' for clinical trial, and '**m**' for meta-analysis. According to the general consensus in EBM, articles marked with **r**'s or **m**'s tend to be top-quality evidence. PubMed allows both '**r**' and '**c**' to be assigned to the same article, hence we may see articles marked with **rc**'s in the map.

TEST EXAMPLES

We illustrate the above features with two test examples: 1) clinical trials regarding risk factors of heart diseases (1990-2004), and 2) systematic reviews of lung cancer (1990-2004). The heart disease dataset consists of 6,235 records. The lung cancer dataset contains 1,618 records. These records are known as citing records. Visualizations represent references cited by these records. Citing records are included if themselves are cited by others.

CiteSpace imports each of the two datasets directly and selects burst terms – terms with sudden surges of popularity – from titles, abstracts, and descriptors of citing records. CiteSpace divides the entire time interval into a number of sub-intervals, or time slices. A snapshot network is derived for each time slice. The resultant time series of networks are subsequently merged into a global network. Technical details of the algorithms are described in [12, 15].

CiteSpace supports two visualization views: cluster views and timezone views. Cluster views show networks as the commonly seen types of node-and-link diagrams, whereas timezone views arrange articles and terms in correspondence to the time of their publication or their peak time.

RESULTS

Figure 2 shows four screenshots of the heart disease example. The overviews are generated with various interactive controls, such as turning on term labels, showing salient paths, and showing the types of evidence. Details of visualizations are shown in subsequent figures. Figure 3 shows the timezone view visualization of the heart disease dataset. Each vertical strip is a time zone. The corresponding year is marked at the bottom of the view, from left to right. The size of a node indicates its frequency if it is a term, or its citations if it is an article. A line between a term and an article denotes that the article is cited by the hosting article of the term. The emerging trends can be identified by the rightmost elements of a cluster. CiteSpace allows the user to select a group of items by dragging a rectangle surrounding area (for example, the 2000 timezone was selected in Figure 2) and the details of selected items are listed in the table below the view.

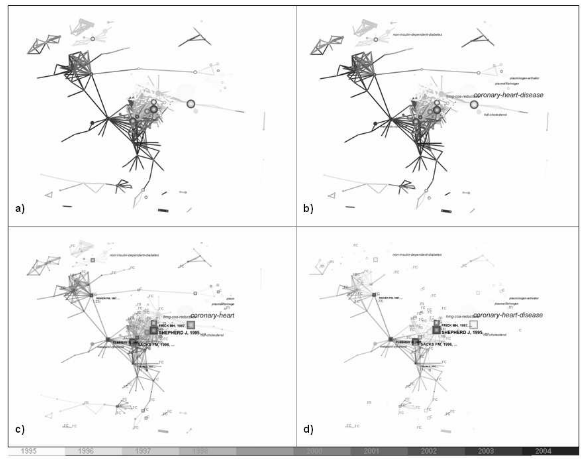

Figure 2. Overviews of the heart disease dataset: a) the network with no annotations; b) with burst terms; c) with evidence types; d) with only the landmark-landmark paths shown. Landmarks are nodes of high *betweenness centrality*, which is defined as the probability that an arbitrary shortest path passes a given node.

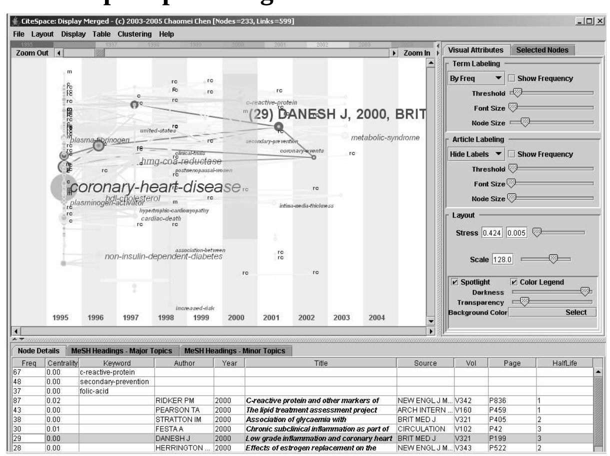

Figure 3. The timezone view of the heart disease example. The network contains 233 vertices and 599 edges. This is a top-cited subset of the entire data.

Figure 4 shows a portion of the cluster view of the lung cancer example. The search query included the term systematic review. The colors indicate different time-stamped connections. The distributions of various types of clinical evidence can be seen from the overview map. An interesting and an indeed unexpected observation is that clinical evidence turned out to be less frequently positioned as hubs and bridges as we originally expected. Nevertheless, meta-analysis articles, as one would expect, tend to cluster tightly with a group of RCTs or clinical trial articles.

Figure 5 shows a screenshot of the lung cancer example. The cluster on the top was formed recently, as shown in the colors of its lines. The cluster is almost uniformly RCTs and includes one meta-analysis by Pignon in 1992. In this view, the spotlight mode highlights the paths connecting nodes with high betweenness centrality and fade out other less important paths. We expect these visual exploration features can help users to identify clinical evidence and assess relevant significance of a specific article more efficiently than sifting through a list of articles.

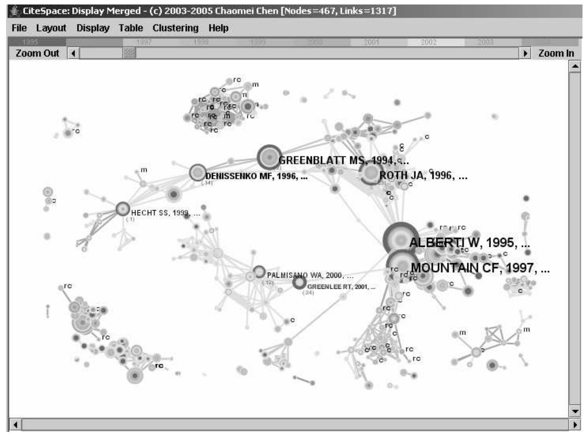

Figure 4. The cluster view of the lung cancer systematic review dataset, containing 467 items and 1,317 links.

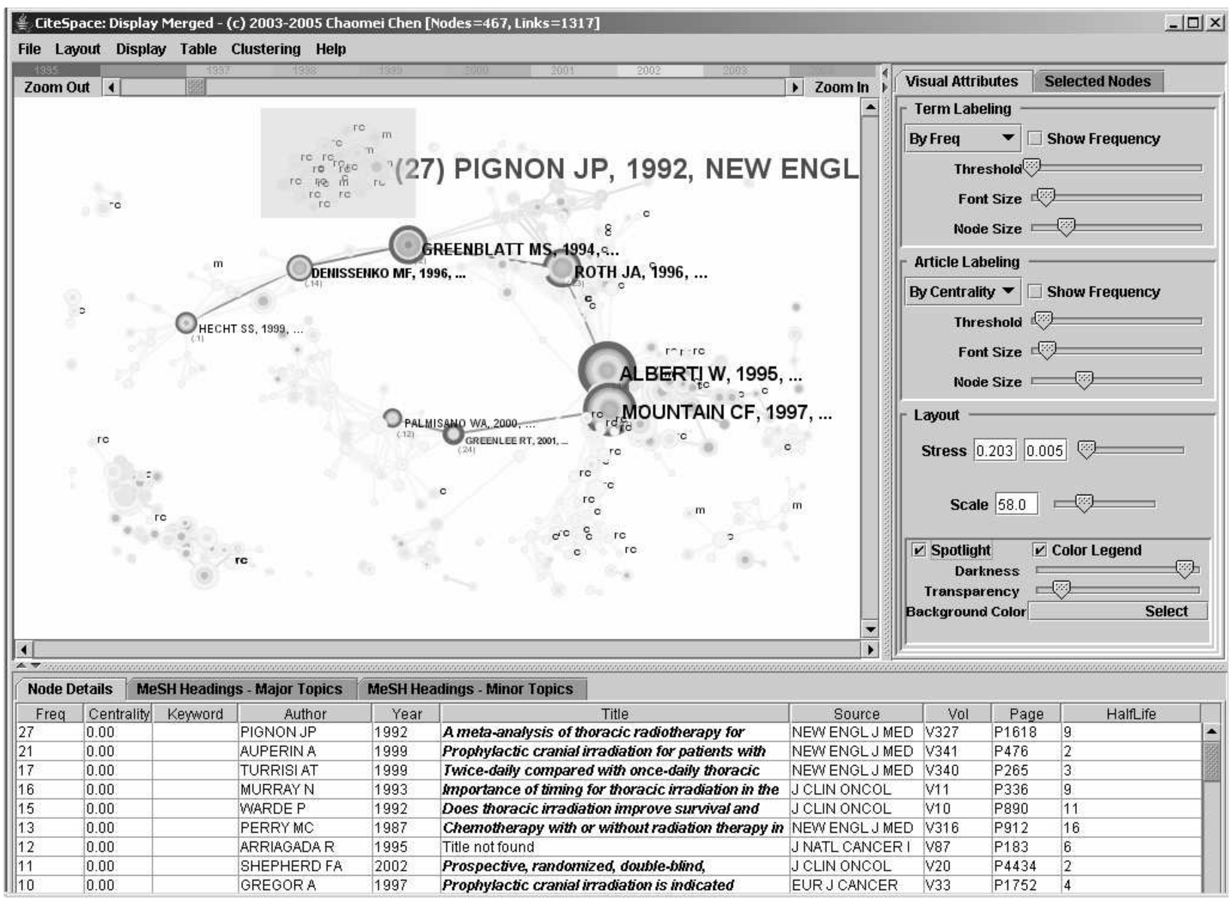

Figure 5. The visualization of the lung cancer systematic review example. The top cluster is selected.

DISCUSSIONS AND CONCLUSIONS

The preliminary results are encouraging because the automatic annotation technique provides a harmonic way to combine two different sources of evidence. It is impractical to expect that scientists and clinicians could keep track of every new development in the fast-advancing life sciences. We expect the tool will significantly improve the cost-effectiveness of searching for clinical evidence in the literature as a crucial step in the practice of EBM. We envisage a wide variety of users could potentially benefit from the provision of such tools, including EBM practitioners in the preparation of systematic reviews, educators and students in medical schools, patients and their friends and families, and ultimately, clinicians and government regulating agencies such as Food and Drug Administration (FDA).

The general design of CiteSpace has been evaluated in a heuristic evaluation [16] and a cognitive walkthrough [17]. More specific evaluations in the context of medical informatics and EBM are being planned for future work as well as validating the results with domain experts and integrating the functionality into other components of the EBM procedure. A significant dimension of future work is to incorporate natural language processing algorithms and identify hypotheses and evidence at sentence levels from abstracts.

It is not our intention to replace traditional methods of searching and appraisal clinical evidence with automated methods. Rather, our goal is to provide tools that can help EBM practitioners so that they can deal with tedious and time-consuming tasks more efficiently and devote more time to critical issues.

Note

CiteSpace and color figures are available at:
http://cluster.cis.drexel.edu/~cchen/citespace

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