



Global Research of the Use of Contrast-Enhanced Ultrasound in Cancer Diagnostic Process: A Bibliometric Analysis and Future Perspective

Rayvita A. N. Meagrata^{1*}, Rayvivant I. Robbyersyadaney¹

1. Department of Basic Medical Sciences, Faculty of Medicine, Universitas Wahid Hasyim, Indonesia

Korespondensi : r.meagrata@unwahas.ac.id

ABSTRAK

Pendahuluan: *Contrast-enhanced ultrasound* (CEUS) dapat digunakan untuk membedakan beberapa jenis tumor ganas. Namun, analisis bibliometrik yang merangkum tren penelitian global dengan topik CEUS untuk mendiagnosis kanker masih terbatas. Penelitian ini bertujuan untuk mengamati tren perkembangan CEUS dalam mendiagnosis kanker dan mengusulkan penelitian di masa depan.

Metode: Analisis bibliometrik dilakukan terhadap data publikasi yang diambil dari database Scopus dengan pencarian kata kunci tertentu. Pencarian data diselesaikan dalam waktu satu hari (1 Juni 2024) untuk menghindari kemungkinan bias akibat mekanisme pembaruan database Scopus secara berkala. Data dibatasi untuk publikasi berupa artikel yang diterbitkan sejak awal publikasi hingga tahun 2023. Data-data berupa profil bibliografi, tren tahunan, dan hotspot penelitian dianalisis dan divisualisasikan menggunakan VOSviewer.

Hasil: Sejak tahun 1994, terdapat peningkatan keluaran publikasi tahunan dari 2605 dokumen yang teridentifikasi dengan tingkat pertumbuhan rata-rata sebesar 2,35%. Tiga negara yang paling produktif terhadap penelitian topik ini yaitu Tiongkok (50,67%), Jepang (10,17%), dan Amerika Serikat (9,21%). “Ultrasound in Medicine and Biology” menerbitkan artikel terbanyak yang berkaitan dengan topik ini. Penelitian di bidang kedokteran (medicine) paling banyak diminati, diikuti penelitian di bidang biokimia, genetika, dan biologi molekuler (biochemistry, genetics and molecular biology). Sebanyak 4032 kata kunci diklasifikasikan ke dalam delapan kelompok termasuk *contrast-enhanced ultrasound*, *breast cancer*, *hepatocellular carcinoma*, diagnosis, liver, *contrast media*, metastasis, dan sonazoid.

Kesimpulan: Studi bibliometrik ini menunjukkan tren global CEUS dalam bidang diagnosis keganasan. Selain biayanya yang rendah dan keunggulan tanpa radiasi, CEUS merupakan modalitas diagnostik yang menjanjikan untuk membedakan lesi ganas. Penelitian pada topik ini masih dapat dikembangkan pada berbagai lokasi dan jenis keganasan.

Kata Kunci: Kanker; *Contrast-enhanced ultrasound*; Diagnostik; Analisis Bibliometrik

ABSTRACT

Background: *Contrast-enhanced ultrasound* (CEUS) imaging has been reported for its role in differentiating several types of malignant tumors. However, there was still limited bibliometric analysis that summarizes the global research trends in the field of CEUS for diagnosing cancer. The present study aimed to observe the trend by which the research field has grown over the years and propose a possible future trend.

Methods: Bibliometric analysis was performed on publications data retrieved from the Scopus database with specific search for keywords. The data search was completed within a day (1 June 2024) to avoid possible bias due to the regular updating mechanism of the Scopus database. Data were limited to publications in the form of articles published from the beginning of publication until 2023. The data including bibliographical profiles, the annual trend, and the study hotspots were analyzed and visualized using VOSviewer.

Results: Since 1994, the annual publication outputs of 2605 identified documents were increased with an average growth rate of 2.35%. The top three most productive countries were China (50.67%), Japan (10.17%), and the United States (9.21%). *Ultrasound in Medicine and Biology* published the most articles related to the subject. The research in the Medicine area was receiving the most interest, followed by Biochemistry, Genetics and Molecular Biology area. A total of 4032 keywords were classified into eight clusters including *contrast-enhanced ultrasound*, *breast cancer*, *hepatocellular carcinoma*, diagnosis, liver, *contrast media*, metastasis, and sonazoid.

Conclusion: *This bibliometric study demonstrated global trends of CEUS in the field of diagnosing malignancy. Besides its low cost and no-radiation advantages, CEUS is a promising diagnostic modality for differentiating malignant lesions. Research in this field can still be developed in a wide range of locations and types of malignancy.*

Keywords: *Cancer; Contrast-enhanced ultrasound; Diagnostic; Bibliometric analysis*

INTRODUCTION

Based on WHO data in 2019, there has been an increase in cancer as a cause of death throughout the world (Sung et al. 2021). Various measures have been taken to reduce the rate, including effective and efficient efforts in establishing the diagnosis. The use of contrast-enhanced ultrasound (CEUS) in cancer management was increasing; some of the reasons including the side effects of radiation could be avoided and it had a better level of accuracy than conventional ultrasonography (Kessner et al. 2019). CEUS imaging has been reported for its role in differentiating malignant lesions (Kuru et al. 2015; Marrero et al. 2018; Ljungberg et al. 2019; Wang et al. 2022). However, there is still limited bibliometric analysis that summarizes the global research trends in the field of CEUS for diagnosing cancer. To fill this gap, a comprehensive bibliometric analysis was conducted based on publications related to CEUS for diagnosing cancer.

In this study, the following questions were mainly addressed: i) global publication trends; ii) major contributors based on the country; iii) most popular journals; iv) main focuses in current research; v) potential research topics in the future. The present study aimed to observe the trend and also provide new ideas and perspectives for the researcher's future work in the field of CEUS for diagnosing cancer.

METHODS

This bibliometric analysis was performed on publications data retrieved from the Scopus database. The data search was completed within a day (1 June 2024) to avoid possible bias due to the regular updating mechanism of the Scopus database. The keywords relevant to CEUS for diagnosing cancer were searched in the publication's title, abstract, and keywords. Only original articles were enrolled without language limitation. The search formula was set as follows: TITLE-ABS-KEY (cancer AND diagnose* AND "Contrast-enhanced ultrasound" OR "Contrast-enhanced ultrasonography") AND PUBYEAR > 1993 AND PUBYEAR < 2024 AND (LIMIT-TO (DOCTYPE , "ar")). To analyze trends on this topic, the articles involved were those published from the beginning to the end of 2023. The wildcard character (*) was used so that the term "diagnose" could be substituted with "diagnosing" or "diagnostic".

The data of publications by year, country, subject area, and journal source was extracted and processed by the Scopus-analysis menu and then downloaded as necessary. The average growth rate was calculated according to the formula described by Guo et al (Guo et al. 2020). The CSV-format data from the Scopus database was downloaded for further analysis and visualization using Vosviewer version 1.6.19. This research conducted keyword co-occurrence analysis of journals. The keywords were taken from the author-supplied keyword list.

RESULT AND DISCUSSION

A total of 2605 documents were obtained from the Scopus database. The analysis was made based on the research questions.

Annual Publication Trend

The first article related to the subject was published in 1994 in the Cardiovascular and Interventional Radiology journal (Veltri et al. 1994). The latest article obtained was published in the Clinical Hemorheology and Microcirculation. The publications in the field of CEUS for diagnosing cancer demonstrate an increase in the number of studies with an average growth rate of 2.41%. The acceleration of research publications started in 2004 with a growth rate of 14.16%, which was also the highest growth rate. The graphic of the annual publication trend was shown in Figure 1.

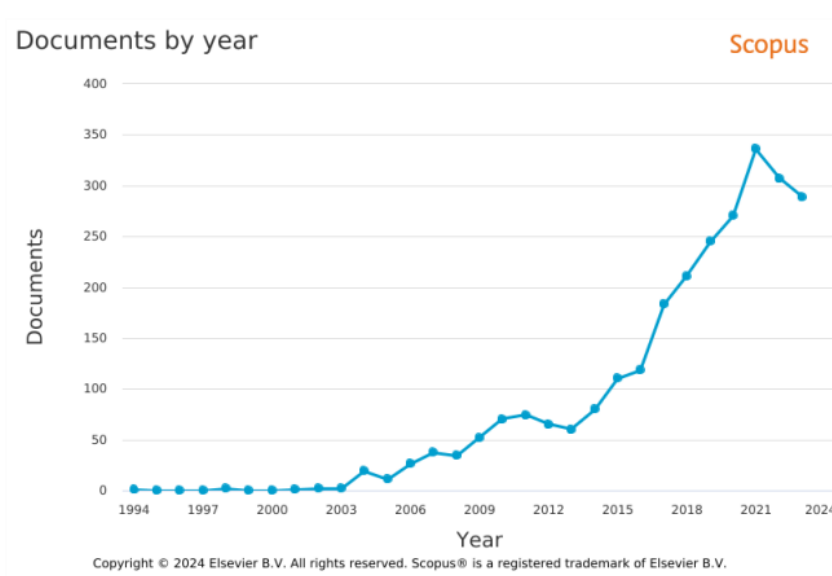


Figure 1. Worldwide research trend of CEUS for diagnosing cancer.

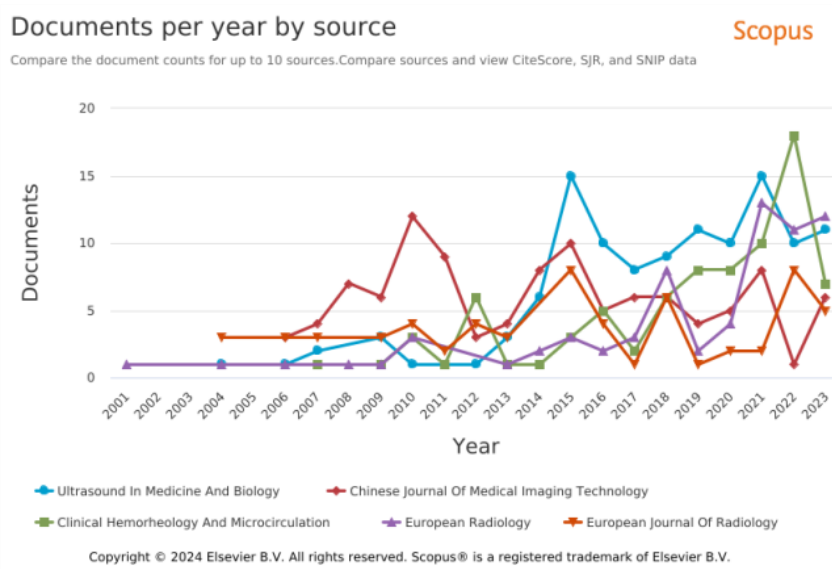


Figure 2. Top ten contributors to publications published related to the subject in the Scopus database

Major Contributors

Data showed that China (50.67%), Japan (10.17%), and the United States (9.21%) were the top three of the most productive countries in the field of CEUS for diagnosing cancer. Three of the top ten productive countries were East Asia countries. Among Southeast Asian countries, only Singapore, Malaysia, Thailand, and Philippines held studies related to the subject (all of them contributed less than 10 articles). The top ten of the most productive countries was summarized in Figure 2.

As reported in a previous study, accounting for 49.3% of world cancer incidents occur in Asia, with a significantly increasing number happened in Korea, Japan, and Kuwait (Huang et al. 2022). The highest cancer incidence among Asian countries was reported in East Asia, while less than one-third of that in East Asia happened in Southeast Asia (Rajappa et al. 2023).

The Ultrasound in Medicine and Biology published the most articles related to the subject (117 articles). Other top five journals were the Chinese Journal of Medical Imaging Technology (107 articles), Clinical Hemorheology and Microcirculation (81 articles), European Radiology (69 articles), and European Journal of Radiology (62 articles). The publication trend of the top three journals was shown in Figure 3.

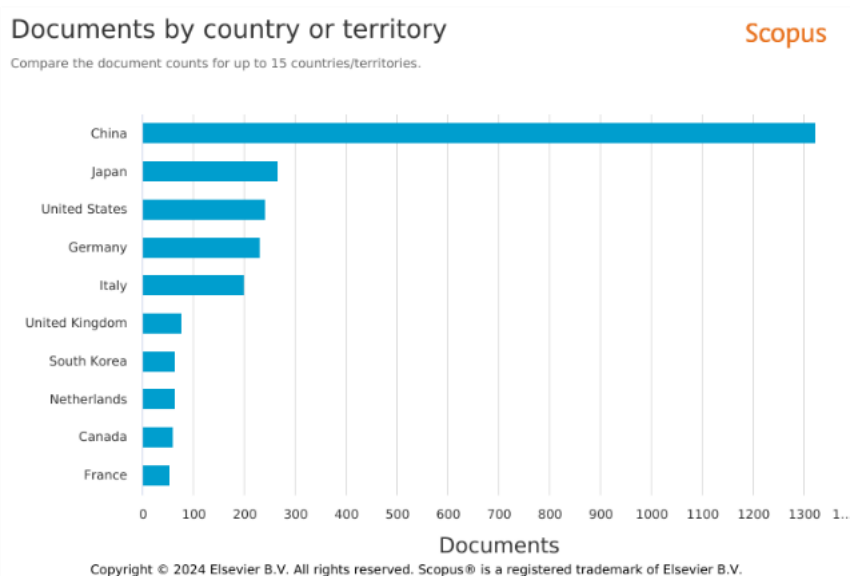


Figure 3. Trend of articles by years by publishing journal.

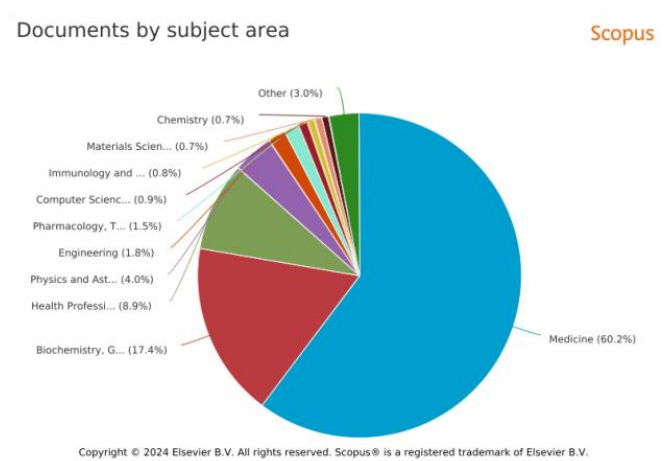


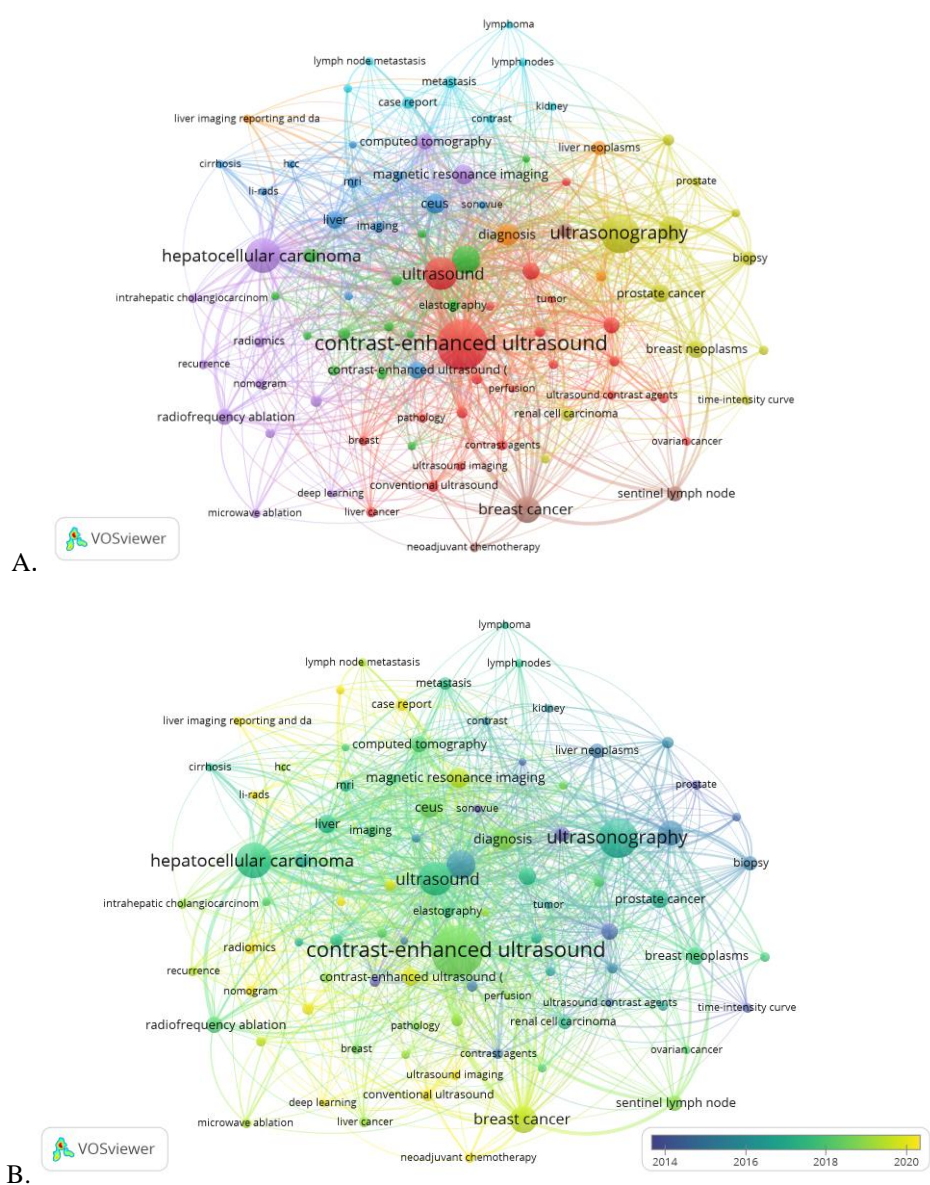
Figure 4. Area of interest related to the subject in the Scopus database.

Most Popular Area of Interest

As shown in Figure 4, the research in the Medicine area was receiving the most interest (60.2%). The Biochemistry, Genetics and Molecular Biology (17.4%) and Health Professions (8.9%) ranked in the second and third place of research areas that received the most interest.

Keyword Co-occurrence Analysis

A minimum of 15 keyword occurrences were established, thus obtaining 88 out of 4032 keywords that met the criteria. Later, the keywords were classified into eight clusters shown in eight different colors. Keyword co-occurrence analysis was displayed in Figure 5 as network, overlay, and density visualization maps. The thickness of the node referred to the occurrences, the thickness of the line referred to the strength of the connection between two keywords, and the distance between each node referred to the relationship of the keywords (Li et al. 2022).



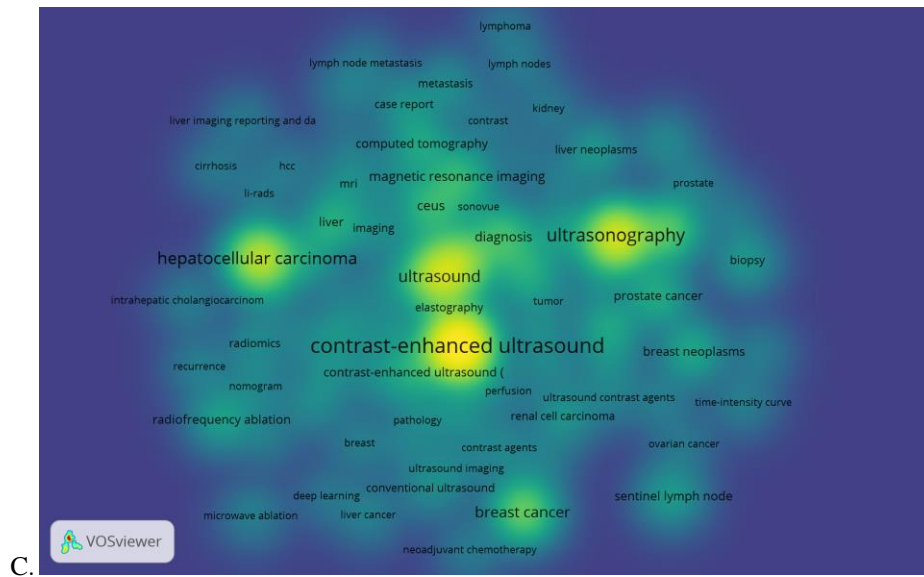


Figure 5: A. Network visualization; B. Overlay visualization; C. Density visualization.

Network Visualization

The network visualization map shows the co-occurrence relations between keywords. (van Eck and Waltman 2014) The term ‘contrast-enhanced ultrasound’ existed in the top three clusters. The first cluster, presented in red color, consisted of 22 keywords as ‘contrast-enhanced ultrasound’ (575 occurrences), ‘ultrasound’ (250 occurrences), and ‘microbubbles’ (62 occurrences) appeared most frequently. ‘Sonazoid’ (48 occurrences), ‘elastography’ (36 occurrences), and ‘colorectal cancer’ (36 occurrences) were predominantly consisted in the second cluster (14 keywords), presented in green color. The top three most frequent among the 12 keywords of the third cluster (dark blue color) were ‘ceus’ (89 occurrences), ‘liver’ (72 occurrences), and ‘mri’ (31 occurrences). The fourth cluster, presented in lime color, consisted of 12 keywords with the terms ‘ultrasonography’ (334 occurrences), ‘contrast media’ (136 occurrences), and ‘prostate cancer’ (74 occurrences) as the most frequent keywords. Presented in purple color, the fifth cluster consisted of 12 keywords with ‘hepatocellular carcinoma’ (279 occurrences), ‘magnetic resonance imaging’ (88 occurrences), and ‘computed tomography’ (62 occurrences) as the most frequent keywords. Term ‘metastasis’ (34 occurrences), ‘lymph nodes’ (19 occurrences), and ‘diagnosis’ (17 occurrences) appeared most frequently in the sixth cluster (8 keywords) presented in light blue color. The seventh cluster, presented in orange color, consisted of 4 keywords, as ‘diagnosis’ (105 occurrences), ‘liver-neoplasms’ (45 occurrences), and ‘meta-analysis’ (25 occurrences) appeared most frequently. The last cluster consisted of 4 keywords, presented in lilac color with ‘breast cancer’ (157 occurrences), ‘sentinel lymph node’ (52 occurrences), and ‘contrast agent’ (48 occurrences) as the most frequent keywords.

Several similar keywords were identified separately in almost all clusters. Some of them were ‘contrast-enhanced ultrasound’, ‘contrast enhanced ultrasound’, ‘contrast-enhanced ultrasound (ceus)’, ‘contrast-enhanced ultrasonography’, and ‘ceus’; ‘ultrasonography’ and ‘ultrasound’; and ‘microbubble’ and ‘microbubbles. The similar keywords should be counted as one keyword whose total link strength and average publication year could be described more precisely.

Overlay Visualization

The color used in the overlay visualization map indicates the average publication year. The lighter the color, the more recent the publication (Li et al. 2022). Most of the keywords used in recently published articles, written followed by its occurrences, cluster and average publication year, were ‘deep learning’ (15, 5th, 2022.27), liver imaging reporting and data system (18, 7th, 2021.17),

papillary thyroid carcinoma (19, 6th, 2021.11), case report (37, 6th, 2021.11), nomogram (26, 5th, 2021.88), and radiomics (29, 5th, 2021.66).

Density Visualization

The density of the keywords was visualized by their font size and the node size. Bigger sizes showed higher total link strength (van Eck and Waltman 2014; He et al. 2020). The keywords with high total link strength were contrast-enhanced ultrasound (849), ultrasonography (546), hepatocellular carcinoma (504).

Organ of Interest

Some neoplasms as keywords were analyzed in this research. The liver neoplasm was studied in the first article obtained in this research, along with ‘carbon dioxide’, ‘microbubbles’, and ‘ultrasound contrast media’ (Veltri et al. 1994). The latest article studied neuroendocrine tumors and pancreatic neoplasms (Jiao et al. 2023). However, because ‘neuroendocrine’ does not meet the minimum occurrence requirements, this keyword was excluded.

The keywords analyzed in this research included breast, liver, prostate, kidney, lymph node, colorectal, gaster, pancreas, gallbladder, ovary, and thyroid organ. Keywords containing liver, breast, and prostate were frequently studied, with 588, 246, and 112 occurrences, respectively. Breast and prostate cancers were the first rank of each sex group for the new cancer cases, while liver cancer was the top five leading cancer organs in the male group and the top ten leading cancer organs in the female group for the estimated death (Siegel et al. 2023). CEUS for diagnosing liver neoplasm has already been implemented in several countries (Galle et al. 2018; Marrero et al. 2018).

The drawbacks of this bibliometric study were the similar terms analyzed as different keywords and only obtained data from a single source. The systematic review followed by a meta-analysis and the use of various bibliometric analyzing tools are essential for further research.

CONCLUSIONS

This bibliometric study demonstrated positive global trends of CEUS in the field of diagnosing malignancy. The leading country in the contribution of the subject was China, and the organ most studied was the liver.

Besides its low cost and no-radiation advantages, CEUS is a promising diagnostic tool for differentiating malignant lesions. Research in this field can still be developed in a wide range of locations and types of malignancy.

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