INTERNAL MEDICINE

□ ORIGINAL ARTICLE □

Japanese Lung Cancer Research Trends and Performance in Science Citation Index

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Abstract

Objective This study was undertaken to explore a bibliometric approach to quantitatively assess current research trends in lung cancer in Japan, using the related literature in the Science Citation Index (SCI) database from 1991 to 2008.

Materials and Methods Articles were analyzed by the scientific output and research performances of individuals, institutes, and collaborative countries with Japan. Distribution of words in the article title, author keywords, and KeyWords Plus in different periods was applied to evaluate research trends by the frequency of keywords used.

Results Keyword analysis indicated that there has been a strategy to connect molecular biology with clinical practice. Researchers in Japan have published high impact articles related to non-small cell and small cell lung cancer.

Conclusion Finally, this study highlights the topics in lung cancer research that are becoming popular in Japan.

Key words: lung cancer, scientometrics, web of science, Japan

(Inter Med 49: 2219-2228, 2010)
(DOI: 10.2169/internalmedicine.49.3687)

Introduction

Lung cancer has long been investigated. In earlier years, information on primary lung cancer (1) and radical surgery for primary lung carcinoma (2) were presented. In Japan, an earlier published article discussed unusual intraluminal processes of capillaries in a case of undifferentiated lung cancer (3). In 1981, Hirayama reported that wives of heavy smokers had a higher risk of developing lung cancer (4). Naruke et al (5) evaluated a new Tumor, Node, Metastasis (TNM) staging system for lung cancer. In subsequent years, high impact studies related to small-cell lung cancer (6) and non-small-cell lung cancer (7, 8) were reported. Epidermal growth factor receptor (EGFR) mutations in lung cancer (9) and clinical and biological features associated with EGFR gene mutations in lung cancers (10) were reported in Japan.

Lung cancer is one of the leading causes of cancer-related death among men and women in the civilized world. Although the long-term outlook for lung cancer patients has not changed significantly (11), there have been steady improvements over the recent decades in surgical techniques (12) and in the role of chemotherapy (13) and radiotherapy (14) in the treatment of lung cancer. Lung cancer research is and will be one of the forefront and hotspot subjects of clinical medical sciences. The 7 major industrial countries (G7: USA, Japan, Germany, Italy, UK, France, and Canada) with USA leading the top, held the top 7 spots of total world production in the field of lung cancer research, along with the domination pattern in the publication in most scientific fields. In this research field, however, Japan ranked second in the recent decade.

The present study was designed to determine the Japanese share of published research in the field of lung cancer from 1991 to 2008. A bibliometric method was used to analyze lung cancer research trends and performances including international collaboration, distribution of institutes and author publications.

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Received for publication March 23, 2010; Accepted for publication July 2, 2010
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Methodology

The data were from the online version of the Science Citation Index (SCI), Web of Science, Philadelphia, PA, USA. According to Journal Citation Reports (JCR), it indexed 6,620 major journals with citation references across 173 scientific disciplines in 2008. All documents from 1991 to 2008 with "Japan" in the address field and which had the following keywords were downloaded: "lung cancer", "lung carcinoma", "lung malignancy", and "lung metastasis". In total, 10,052 publications met the selection criteria. These publications were check to determine whether they were published by Japan; eighteen publications were excluded which used "Japan" in the address for example, China-Japan Friendship Hospital in China; China-Japan Union Hospital of Jilin University at China; Kuakini Medical Center, and Japan-Hawaii Cancer Study in USA.

Document information included names of authors, titles, years of publication, source journals, contact addresses, and subject categories of journals. The records were downloaded using Microsoft Excel software, and additional coding was manually performed for the number of authors, origin countries and institutes of the collaborators, and impact factors of the source journals. Impact factors were taken from the Journal Citation Report (JCR) published in 2008. Contributions of different institutes and countries were estimated by the affiliation of at least one author to the article. Articles originating from England, Scotland, Northern Ireland, and Wales were reclassified as from the United Kingdom (UK). Articles from Hong Kong were not included in China. Collaboration type was determined by the addresses of the authors, where the term "Japan independent article" was assigned if the researchers' addresses were all from Japan. The term "internationally collaborative article" was designated to those articles that were coauthored by researchers from multiple countries. The term "institute independent article" was assigned if the researchers' addresses were from the same institute in Japan. The term "inter-institutionally collaborative article" was assigned if authors were from different institutes. The emphasis of the following discussion was to determine the scientific performances and research activity trends which consisted of categories, journals, institutes and countries distributions; and the trends in research topics were addressed.

Results and Discussion

Document type and language of publication

The distribution of the document type identified by the Institute for Scientific Information (ISI) was analyzed. Eleven document types were found in the total 10,034 publications during the 18-year study period. Article (8,373) was the most-frequently used document type comprising 83% of the total publications, followed distantly by meeting abstracts (661; 6.6%), proceedings papers (661; 3.5%), and reviews (283; 2.8%). The others showing less significance were letters (169), notes (122), editorial materials (72), discussions (3), corrections (2), new item (1), and addition correction (1). As journal articles represented the majority of document types that also included whole research. Only 8,373 articles were used for further analysis. Almost all of these articles (8,251) were published in English. Three other languages also appeared, including Japanese with 20 articles and one for Korean and Russian.

Trend of articles

The total of Japanese articles in SCI including the search words "lung cancer", "lung carcinoma", "lung malignancy", and "lung metastasis" during the last 36 years was counted (Fig. 1). A development trend was found for all documents and articles, searched by titles, keywords, and abstracts, which increased from 3 in 1973 to 777 publications in 2008 and 3 in 1973 to 646 articles in 2008. According to a limitation of the SCI database, since 1991, abstract information has been included in it. However, the topic search can trace the related information in titles, abstracts, and keywords at one time. Thus searching keywords in titles only is necessary to obtain a reasonable base for the years before 1991. A similar trend also appeared for all documents and articles, searched by titles only, which increased from 3 in 1973 to 310 publications in 2008 and 2 in 1973 to 237 articles in 2008. In the last 18 years, the number of articles devoted to lung cancer research increased more than four-fold, from 191 in 1991 to 696 in 2006. It is clear that a decreasing trend was found during last three years. Same trend was observed with articles published in impact factor (IF$\geq$3) journals. Along with the Japanese development of SCI articles, lung cancer research continually grew in this period, which started to increase significantly in the 1980s and rocketed after 1990. Japan had important contributions in lung cancer research during 1991 to 2008. For example, Dr. Y. Fujii at Nagoya City University Medical School, published the most cited paper "EGFR mutations in lung cancer: correlation with clinical response to Gefitinib therapy" and Dr. M. Fukuoka at Kinki University with an international team published "multi-institutional randomized phase II trial of Gefitinib for previously treated patients with advanced non-small-cell lung cancer". In 1984, the Japanese government started the 3rd 10-year project for cancer. In 1990, the Japan Clinical Oncology Group (JCOG), a collaboration group of many institutions, facilitated by public research funds subsidized by Ministry of Health, Labor and Welfare cancer research grants and public welfare labor science research funds, was established. JCOG taught appropriate research methodology to physicians through a well-designed curriculum (15). In addition a high impact article related to small-cell lung cancer was published by the Japan Clinical Oncology Group (16). Several lung cancer study groups such as the West Japan Oncology Group were established subsequently. Recently, systematic education of medical oncology includ-

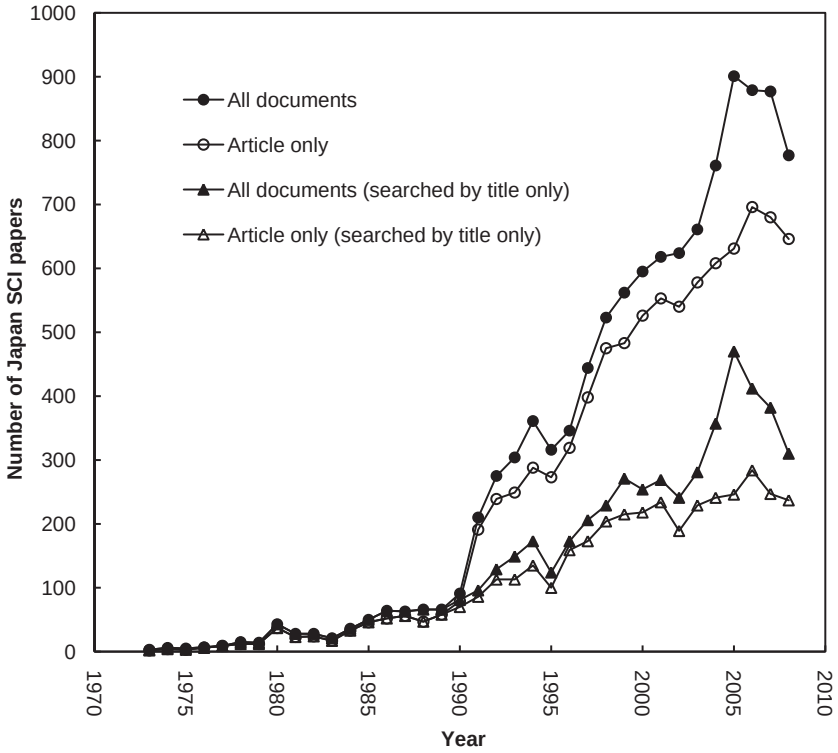

Figure 1. **Number of Japanese publications in SCI referring to keywords "lung cancer", "lung carcinoma", "lung malignancy", and "lung metastasis" during last 36 years.**

ing the systematic training program of "clinical research methodology" at the undergraduate level has been started at many academic teaching institutions. Such efforts have effectively promoted the development of Japan lung cancer research. Lung cancer research in Japan is still developing, although some research has attained the international level.

Distribution of output in subject categories and journals

Based on the classification of subject categories in JCR 2008, the article output data was grouped into 106 SCI subject categories. The annual articles of the top 5 productive subject categories were analyzed and are shown in Fig. 2. The number of scientific articles per category exhibited constant growth during this period, which indicated that Japanese lung cancer research had been steadily developing in various categories. The distribution of subject categories showed that Japanese lung cancer research covered not only clinical but also basic science research. Oncology held the primary position all through the study period as it was a typical field for lung cancer research. The following study area showing an increasing trend was respiratory system.

In total, 8,373 articles were published in 854 journals. *Lung Cancer* published the most articles with 376 articles comprising 4.5% of all the articles, followed by *Anticancer Research* (4.1%), *Cancer Research* (3.6%), *Oncology Reports* (3.1%), and *Japanese Journal of Cancer Research* (3.1%).

International collaboration

The collaboration with different countries was estimated by the location of the affiliation of at least one author of the published papers. Of all the 8,373 articles with author addresses, 7,194 (86%) were Japan independent articles and 1,179 (14%) were internationally collaborative articles. The results demonstrated Japanese strong independent research ability and less desire to collaborate with other institutes in lung cancer research. Similarly a high percentage of internationally collaborative articles (20%) was also found in stroke-related research in Taiwan (17). Table 1 lists the top 10 internationally collaborative countries ranked by the number of articles with Japan, and the number of internationally collaborative articles, the rank of the total internationally collaborative articles, together with the number and rank of first author articles and corresponding author articles. Domination in collaborative country was the USA followed by China. South Korea had more first and corresponding author articles with Japan. It may be interpreted that such studies were joint research with a country of people who had a similar social background to Japan and a similar genetic background. An increasing trend was found for articles which were published with China (Fig. 3). The most high impact collaborative articles were collaboratively published with the USA (6, 8, 9, 18).

Institutional comparisons

The contributions of Japanese different institutes were estimated by the affiliation of at least one author. The remain-

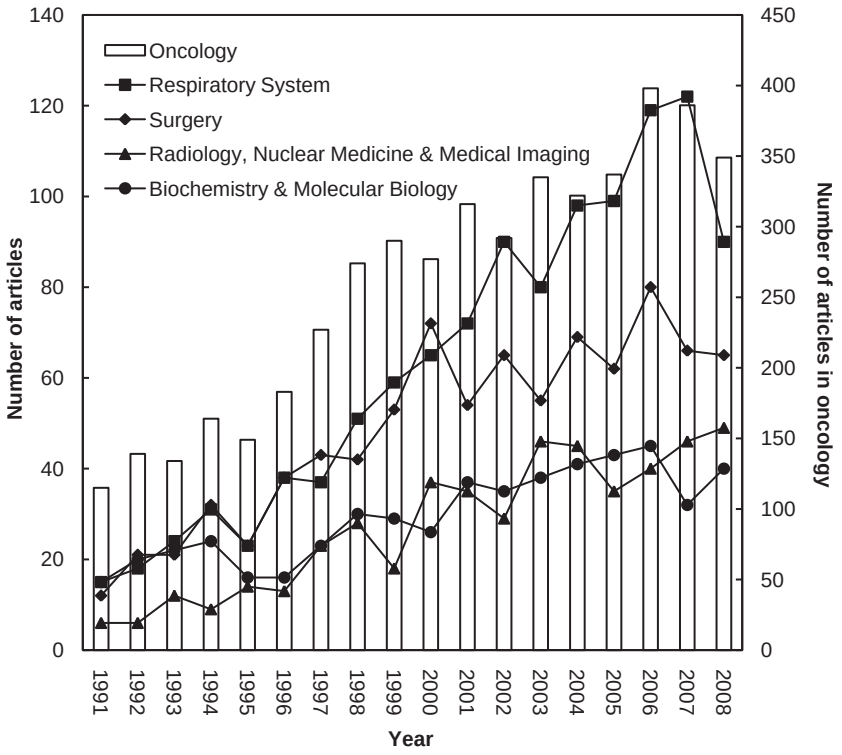

Figure 2. **Comparison of the growth trends of the top five productive subject categories.**

Table 1. **Top 10 Most Internationally Collaborative Countries**

Country	R (CP)	R (FA)	R (RP)
USA	1 (772)	1 (361)	1 (328)
China	2 (102)	3 (25)	5 (23)
UK	3 (69)	6 (17)	6 (15)
France	4 (67)	3 (25)	4 (24)
Germany	5 (65)	5 (20)	3 (26)
South Korea	6 (61)	2 (28)	2 (27)
Italy	7 (38)	8 (12)	8 (12)
Sweden	8 (37)	11 (8)	10 (8)
Canada	9 (35)	7 (13)	7 (13)
Australia	10 (33)	17 (4)	13 (6)

R, rank; CP, internationally collaborative articles; FA, first author articles; RP, corresponding author articles.

ing 8,373 articles were published by 2,266 Japanese institutes that collaborated with 995 overseas institutes. Of the 8,373 articles with Japan author addresses, 3,525 (42%) were independent articles and 4,848 (58%) were inter-institutionally collaborations of two or more institutes. The top 20 institutes were ranked by the number of articles, including the number and percentage of single institute articles and inter-institutionally collaborative articles, as well as first and corresponding author articles (Table 2). The National Cancer Center had the most total articles with 710 articles, followed by Kyushu University with 400 articles, The University of Tokyo with 339 articles, Okayama University with 310 articles, and Kyoto University with 304 articles. The National Cancer Center published not only the most total articles, it also completed the most independent and inter-institutionally collaborative articles. Moreover, the first author and corresponding author of articles from The National Cancer Center ranked the highest. It was important that the budget of the project invested in these institutions, and researchers who tried to promote the project gathered there. Among the top 20 institutes, 3 were not universities including The National Cancer Center, Aichi Cancer Center, and The National Cancer Center Hospital East. In terms of lung cancer-related research, universities performed very well in Japan. While the University of Tokyo and Aichi Cancer Center have higher total articles and percentage of inter-institutionally collaborative articles in total institute articles (C%), they may have extensive research networks and

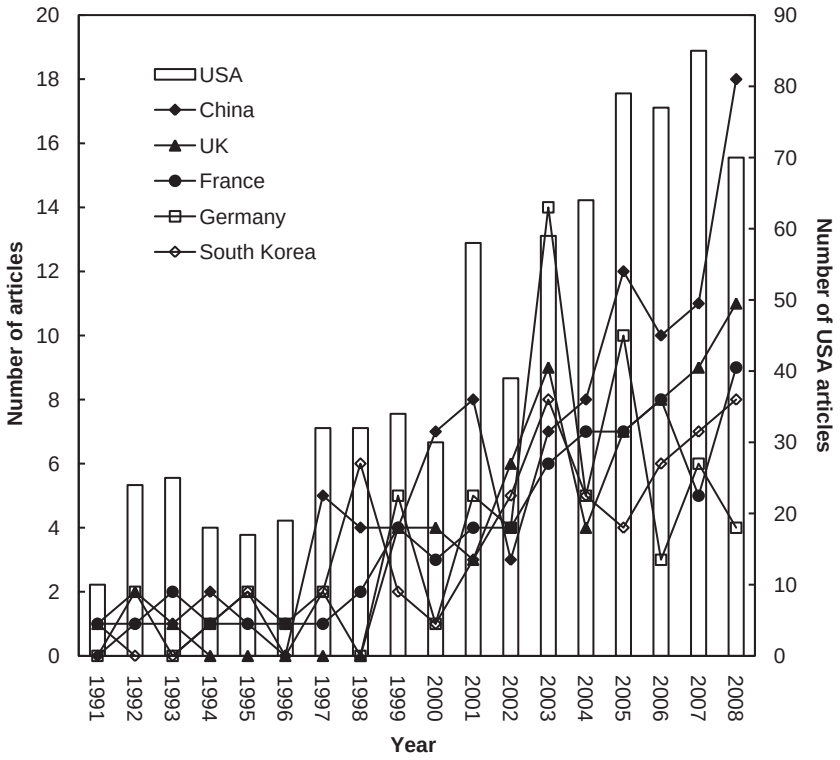

Figure 3. **Top six most collaborative countries.**

many collaborators (17). However, the University of Tokushima is more inclined or able to conduct research independently with 56% of collaborative articles in total articles. The ratio of inter-institutionally collaborative articles' to total articles of institutes was higher than 50%, which indicated that lung cancer research in Japan called for teamwork and collaboration among different institutes. Furthermore, articles published in high impact factor (IF≥3) journals were also analyzed and are listed in Table 2. The National Cancer Center still led the top in all indicators in the high impact factor journals. Aichi Cancer Center (68% of all articles published in the institute) and University of Tokyo (63%) had a higher percentage of the high impact factor journal articles, however Okayama University had a lower percentage (40%) of high impact factor journal articles.

Distribution of authors

The average number of authors per article, from 1991 to 2008, was 7.6 with 66 as the largest number of authors. The 8,373 published articles were coauthored by 15,650 authors, of which 8,461 authors (54%) contributed to only 1 article, 2,436 (16%) 2 articles, 1,207 (7.7%) 3 articles, and 666 (4.3%) 4 articles. Lotka (1926) (19) reported a relationship

$x^n y=c$, (1)

where x is the number of articles, y is the number of authors publishing x articles, n is an exponent which was normally in a value between 1 and 2, and c, a constant depending on the specific field is the number of authors who published only one article. Higher n means a higher distribution of authors who published more articles in a research topic. Lotka law was applied to describe the relationship between the number of articles in Japan lung cancer research and the number of authors making the specified number of articles. Determined by a trial-and-error procedure for the non-linear method using the solver add-in with Microsoft's spreadsheet, Microsoft Excel, the constants c and n in Eq. (1) could be determined from the first 20 points, which were found to be 10,834 and 1.90. Thus, the general Lotka model for the relation was found to exist between the frequency y of researchers making x articles published in Japan lung cancer research field in 1991 to 2008, which can be written as:

$x^{1.90}y=10{,}834$ (2)

or

$x=133y^{-0.526}$ (3)

Figure 4 shows a significant correlation between the number of articles in Japanese lung cancer research and the number of authors making the specified number of articles with the Lotka model. Furthermore, for the special case of the Lotka law whereby n=2, the inverse square law of scientific productivity is also presented in Fig. 4 for a reason of comparison. The relationship of authors to articles for dental science literature was reported to be $1/n^{1.95}$.

In general, the most support of profession and funding for a paper is from the corresponding author. An analysis of the corresponding authors (reprint authors), institutes, and the countries was undertaken for the articles. A total of 7,668 articles with records of reprint authors in the ISI were analyzed. Ninety-three percent (7,118) of total reprint author articles were published by Japan. Only one article per Japan investigator was published by 59% (1,565) of corresponding authors, whereas 16% (427) of corresponding authors had

Table 2. The Top 20 Most Productive Japan Institutes on Lung Cancer Research

Institute	TP	TP3 (R)	TPR (%)		IPR (%)		CPR (%)		FPR (%)		RPR (%)		C%
			TP	TP3	IP	IP3	CP	CP3	FP	FP3	RP	RP3	
National Cancer Center	710	394 (55)	1 (8.5)	1 (11)	1 (4.5)	1 (5.4)	1 (11)	1 (14)	1 (5.9)	1 (7.4)	1 (5.0)	1 (6.4)	77
Kyushu University	400	191 (48)	2 (4.8)	3 (5.4)	2 (3.7)	2 (4.9)	3 (5.6)	7 (5.6)	2 (3.0)	2 (3.5)	2 (2.9)	2 (3.3)	68
University of Tokyo	339	214 (63)	3 (4.0)	2 (6.0)	23 (1.1)	12 (1.6)	2 (6.2)	2 (8.2)	12 (1.7)	5 (2.5)	13 (1.6)	4 (2.5)	89
Okayama University	310	123 (40)	4 (3.7)	11 (3.5)	3 (2.8)	17 (1.2)	9 (4.4)	9 (4.6)	3 (2.5)	8 (2.2)	3 (2.7)	6 (2.4)	68
Kyoto University	304	178 (59)	5 (3.6)	4 (5.0)	9 (1.9)	4 (3.1)	4 (4.9)	5 (5.9)	4 (2.1)	3 (3.0)	7 (1.9)	3 (2.6)	78
Osaka University	297	176 (59)	6 (3.5)	5 (5.0)	10 (1.8)	6 (2.8)	6 (4.8)	4 (6.0)	10 (1.8)	4 (2.5)	9 (1.8)	5 (2.5)	78
Nagoya University	291	170 (58)	7 (3.5)	6 (4.8)	12 (1.8)	7 (2.7)	7 (4.7)	6 (5.8)	7 (1.9)	6 (2.4)	10 (1.7)	8 (2.3)	79
Hokkaido University	280	139 (50)	8 (3.3)	8 (3.9)	11 (1.8)	11 (1.8)	8 (4.5)	8 (4.9)	5 (2.0)	9 (2.2)	4 (2.0)	8 (2.3)	77
Tohoku University	269	131 (49)	9 (3.2)	9 (3.7)	7 (2.2)	10 (2.1)	10 (3.9)	10 (4.5)	8 (1.9)	10 (1.9)	6 (1.9)	10 (2.0)	71
Chiba University	256	124 (48)	10 (3.1)	10 (3.5)	4 (2.7)	3 (4.0)	11 (3.3)	14 (3.3)	6 (2.0)	7 (2.2)	5 (1.9)	7 (2.3)	63
Aichi Cancer Center	245	166 (68)	11 (2.9)	7 (4.7)	89 (0.26)	92 (0.17)	4 (4.9)	3 (6.9)	18 (1.2)	11 (1.9)	20 (1.0)	14 (1.6)	96
Kanazawa University	237	110 (46)	12 (2.8)	12 (3.1)	5 (2.5)	9 (2.2)	13 (3.1)	11 (3.6)	11 (1.7)	13 (1.5)	7 (1.9)	13 (1.7)	63
Gunma University	206	85 (41)	13 (2.5)	16 (2.4)	13 (1.7)	14 (1.5)	14 (3.0)	15 (2.8)	15 (1.3)	19 (0.87)	15 (1.3)	18 (0.93)	70
University of Tokushima	197	87 (44)	14 (2.4)	15 (2.5)	6 (2.5)	5 (2.9)	18 (2.3)	21 (2.2)	9 (1.9)	11 (1.9)	11 (1.7)	11 (1.8)	56
University of Occupational and Environmental Health	189	89 (47)	15 (2.3)	14 (2.5)	8 (2.0)	8 (2.2)	17 (2.5)	19 (2.6)	13 (1.4)	14 (1.3)	12 (1.6)	12 (1.7)	63
National Cancer Center Hospital East	184	98 (53)	16 (2.2)	13 (2.8)	25 (1.0)	15 (1.3)	12 (3.1)	12 (3.5)	20 (1.1)	15 (1.2)	19 (1.0)	15 (1.2)	82
Hiroshima University	178	74 (42)	17 (2.1)	19 (2.1)	16 (1.5)	33 (0.86)	15 (2.6)	18 (2.7)	16 (1.3)	20 (0.85)	16 (1.3)	19 (0.87)	70
Nagasaki University	155	55 (35)	18 (1.9)	25 (1.6)	17 (1.4)	17 (1.2)	19 (2.2)	27 (1.7)	17 (1.2)	16 (1.0)	17 (1.1)	16 (1.0)	68
University of Tsukuba	152	52 (34)	19 (1.8)	27 (1.5)	14 (1.6)	40 (0.69)	23 (2.0)	24 (1.8)	14 (1.3)	22 (0.82)	14 (1.4)	19 (0.87)	63
Nagoya City University	146	59 (40)	20 (1.7)	22 (1.7)	15 (1.6)	15 (1.3)	25 (1.9)	24 (1.8)	19 (1.1)	32 (0.70)	17 (1.1)	30 (0.75)	62

TP, total articles; TP3, total articles (impact factor ≥ 3); R, percentage of total articles (impact factor ≥ 3) in a institute; TPR, total article rank; IP, independent articles; IP3, independent articles (impact factor ≥ 3); IPR, independent article rank; CP, inter-institutionally collaborative articles; CP3, inter-institutionally collaborative articles (impact factor ≥ 3); CP, inter-institutionally collaborative articles; CP3, inter-institutionally collaborative articles (impact factor ≥ 3); CPR, inter-institutionally collaborative article rank; FP, first author articles; FP3, first author articles (impact factor ≥ 3); FPR, first author article rank; RP, corresponding author articles; RP3, corresponding author articles (impact factor ≥ 3); RPR, corresponding author article rank; % share in total articles; C% percentage of inter-institutionally collaborative articles in total institute articles.

contributed two articles. There were 7,118 articles from 2,674 Japanese corresponding authors who were from 814 Japanese institutes. Of the 814 institutes that published articles on lung cancer, 474 (58%) institutes had only one article with corresponding authors. Furthermore, Table 2 shows that 386 corresponding author articles were addressed in the National Cancer Center followed by Kyushu University (224) and the University of Tokyo (204).

Research emphasis: words in title, author-chosen keywords, and KeyWords Plus

The title of an article always includes the information which the authors would most like to express to their readers, because it would be seen by all readers first. Author keywords analysis offers the information of research trends as viewed by researchers (21). KeyWords Plus provides search terms extracted from the titles of papers cited in the article according to the ISI database (21). In recent years, using the results of distributions of words in the title, author keywords, and KeyWords Plus in different periods have been presented to evaluate research treads (22, 23). All of the single words in the titles of Japanese lung cancer research-related articles were statistically analyzed. As a result, 20 of the most frequently used substantives in titles are shown in Table 3 in 3 six-year periods. Some words are of no use for the analysis of research trends such as prepositions, articles, and conjunctions, which were discarded in this analysis. Therefore, other than the terms “lung”, “cancer”, “carcinoma”, and “lung-cancer” which were searching words, “cell”, “human”, “patients”, and “expression” were the most frequently used single words in titles. “Phase”, “non-small”, “small”, “receptor”, “prognostic”, and “growth” in titles showed a notable increasing trend. However, the terms “p53”, “chemotherapy”, and “human” in titles showed a decreasing trend during the study period.

The analysis of author keywords revealed that 11,058 author keywords were used in 6,125 articles from 1991 to 2008. Table 4 shows the 20 most frequently used author keywords with their rankings and percentages. The three most frequently used author keywords were “non-small cell lung cancer”, “prognosis”, and “immunohistochemistry”. It is clear that authors used both “non-small cell lung cancer”

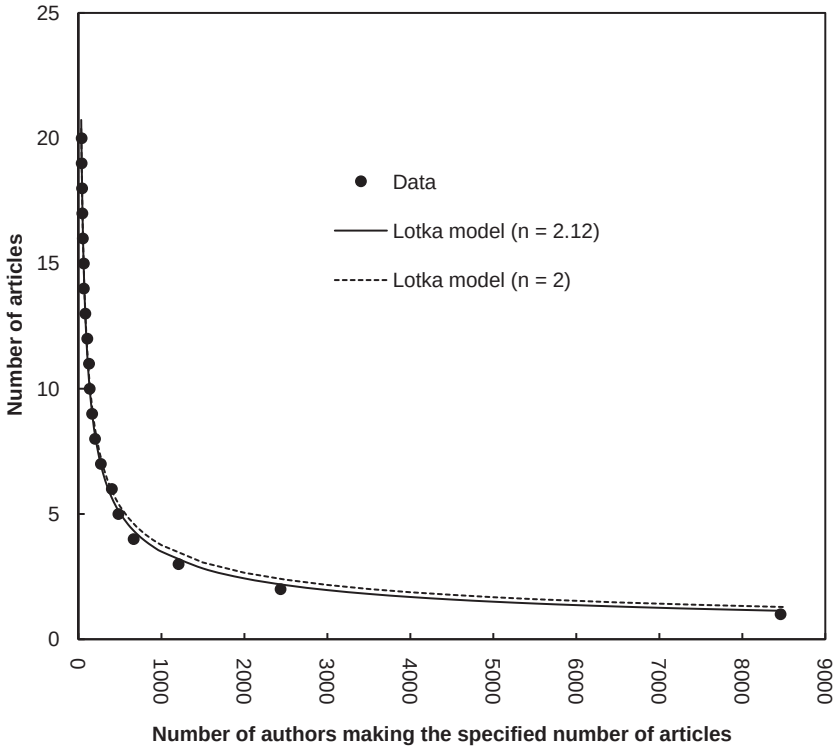

Figure 4. **Relationship between the number of articles and the number of authors publishing the specified number of articles.**

and "non-small-cell lung cancer" as keywords. "Non-small cell lung cancer" was used the most and became popular. "Lung", "cancer", "metastasis", "p53", "adenocarcinoma", and "chemotherapy" were also listed as frequently used words in titles (Table 4). "EGFR", "mutation", "irinotecan", "apoptosis", "paclitaxel", and "non-small cell lung cancer" had higher increasing rates in the ranking of frequency.

The KeyWords Plus in the Science Citation Index (SCI) and Social Science Citation Index (SSCI) database is "an inventive application of the unique power of citation indexing" (21). KeyWords Plus are words or phrases that may be present for articles that have no author keywords or may include important terms not listed among the titles. In recent years, KeyWords Plus were separated into different year periods to analyze the variations of trends on research topics of pentachlorophenol (24), aerosol (22), and stem cell (23). KeyWords Plus were analyzed to substantially augment author-keyword and title-word indexing. Except for "cell lung-cancer", "survival", "breast-cancer", "tumors", "therapy", "mutations", "identification", "in-vivo", "activation", "trial", "lines", "gene-expression", "inhibition", "carcinomas", "in-vitro", and "colorectal-cancer" all other 14 words listed in the top 30 of KeyWords Plus also appeared in the top 30 of author keywords and words in titles. Again, "in-vitro", "in-vivo", "angiogenesis", "apoptosis", "colorectal-cancer", "trial", and "gene-expression" exhibited a rapidly growing pace in Japan lung cancer research. In addition, "metastasis", "adenocarcinoma", and "chemotherapy" appeared in the top 30 of words in titles, author keywords, and KeyWords Plus.

From the analysis of three types of the above keywords, research emphasis and trends could be roughly found. Considering Japanese lung cancer-related research articles, after analyzing the distribution of the three types of the keywords, we summed up the research hotspots into 12 topics: "non-small cell and small cell lung cancers", "metastasis", "chemotherapy", "prognosis", "apoptosis", "Gefitinib", "surgery", "cisplatin", "immunohistochemistry", "p53", "angiogenesis", and "irinotecan" related research. Articles concerning these keywords were analyzed and the distribution of these articles is shown in Fig. 5, 6. The hotspots could be reflected by some highly cited articles. Taking "EGFR" and "Gefitinib" related research for instance, in 2004, "EGFR mutations in lung cancer: correlation with clinical response to Gefitinib therapy" was reported (9). After 2004, a sharply increasing trend appeared. Topics related to non-small-cell lung cancer were introduced in studies such as, "phase III study of concurrent versus sequential thoracic radiotherapy in combination with mitomycin, vindesine, and cisplatin in unresectable stage III non-small-cell lung cancer" (7) and "multi-institutional randomized phase II trial of Gefitinib for previously treated patients with advanced non-small-cell lung cancer" (8). Itoh et al (25), reported "reduced angiogenesis and tumor progression in gelatinase A-deficient mice".

Conclusions

In this study dealing with lung cancer SCI journal papers, we obtained some significant points on Japanese lung cancer

Table 3. Top 20 Most Frequency Substantives in Source Titles during 1991-2008 and 3 Six-year Periods

Words in title	TP	91-08 R (%)	91-96 R (%)	97-02 R (%)	03-08 R (%)
Lung	3,669	1 (44)	3 (20)	1 (51)	1 (48)
Cancer	3,348	2 (40)	4 (13)	2 (45)	2 (47)
Cell	2,032	3 (24)	6 (10)	3 (27)	3 (28)
Human	1,257	4 (15)	2 (22)	4 (17)	9 (11)
Patients	1,166	5 (14)	5 (11)	7 (14)	4 (15)
Carcinoma	1,007	6 (12)	10 (7.1)	5 (14)	6 (12)
Expression	992	7 (12)	8 (7.8)	6 (14)	7 (12)
Cells	864	8 (10)	12 (5.7)	8 (11)	8 (11)
Non-small	808	9 (9.7)	72 (1.7)	10 (10)	5 (13)
Gene	770	10 (9.2)	9 (7.3)	9 (10)	10 (9.1)
Tumor	573	11 (6.8)	15 (4.7)	11 (7.5)	12 (7.2)
Growth	558	12 (6.7)	46 (2.2)	13 (6.7)	11 (8.4)
Study	540	13 (6.4)	13 (5.4)	15 (6.2)	14 (7.1)
Factor	528	14 (6.3)	19 (4.0)	14 (6.4)	13 (7.2)
Metastasis	506	15 (6.0)	14 (5.3)	12 (7.1)	15 (5.5)
Lung-cancer	455	16 (5.4)	1 (29)	889 (0.17)	2203 (0.052)
Pulmonary	416	17 (5.0)	25 (3.3)	17 (5.3)	17 (5.4)
Protein	349	18 (4.2)	23 (3.7)	18 (4.7)	22 (4.0)
P53	346	19 (4.1)	11 (6.7)	16 (5.5)	68 (2.0)
Small	340	20 (4.1)	65 (1.8)	18 (4.7)	18 (4.5)

TP: the number of total articles; R (%): the rank and percentage of words in titles in total articles.

Table 4. Top 20 Frequency of Key Words Used

Key words	TP	91-08 R (%)	91-96 R (%)	97-02 R (%)	03-08 R (%)
Lung cancer	1,454	1 (24)	1 (25)	1 (24)	1 (23)
Non-small cell lung cancer	363	2 (5.9)	30 (1.1)	2 (5.8)	2 (7.7)
Prognosis	262	3 (4.3)	8 (3.1)	3 (4.7)	3 (4.3)
Immunohistochemistry	242	4 (4.0)	4 (4.6)	5 (4.0)	7 (3.7)
Chemotherapy	229	5 (3.7)	6 (3.5)	6 (3.9)	6 (3.7)
Metastasis	213	6 (3.5)	2 (4.9)	7 (3.8)	8 (2.7)
P53	208	7 (3.4)	6 (3.5)	4 (4.5)	10 (2.5)
Apoptosis	207	8 (3.4)	98 (0.41)	9 (3.5)	5 (4.3)
Cisplatin	194	9 (3.2)	5 (3.6)	8 (3.7)	9 (2.6)
Non-small-cell lung cancer	134	10 (2.2)	9 (2.5)	11 (2.0)	12 (2.3)
Small cell lung cancer	129	11 (2.1)	3 (4.7)	14 (1.9)	24 (1.4)
Gefitinib	124	12 (2.0)	N/A	N/A	4 (4.3)
Angiogenesis	110	13 (1.8)	60 (0.62)	10 (2.4)	19 (1.7)
Lung carcinoma	109	14 (1.8)	10 (2.3)	11 (2.0)	23 (1.5)
Adenocarcinoma	103	15 (1.7)	20 (1.4)	18 (1.4)	13 (2.0)
Lung metastasis	99	16 (1.6)	15 (1.6)	11 (2.0)	28 (1.3)
Irinotecan	94	17 (1.5)	234 (0.21)	15 (1.8)	18 (1.8)
Gastric cancer	88	18 (1.4)	38 (0.93)	16 (1.5)	21 (1.6)
Surgery	87	19 (1.4)	17 (1.5)	25 (1.1)	20 (1.6)
Cancer	86	20 (1.4)	30 (1.1)	43 (0.79)	13 (2.0)
Carboplatin	86	20 (1.4)	17 (1.5)	16 (1.5)	28 (1.3)

TP: articles in the study period; R (%): the rank and percentage of the author keyword; N/A: not available

research trends and performances from 1991 to 2008. This study provided a systematically structural picture, as well as clues to the impact of various lung cancer research topics. There was a total of 854 journals listed in the 106 SCI subject categories. The highest number of articles was in *Lung Cancer* and in the subject category of oncology. The USA ranked first in internationally collaborative articles with Japan. The National Cancer Center was the flagship in lung cancer research in Japan, distinctly followed by Kyushu University. Japan has strongly independent research ability. Research collaborative papers shifted from national inter-institutional to international collaboration. Lung cancer re-

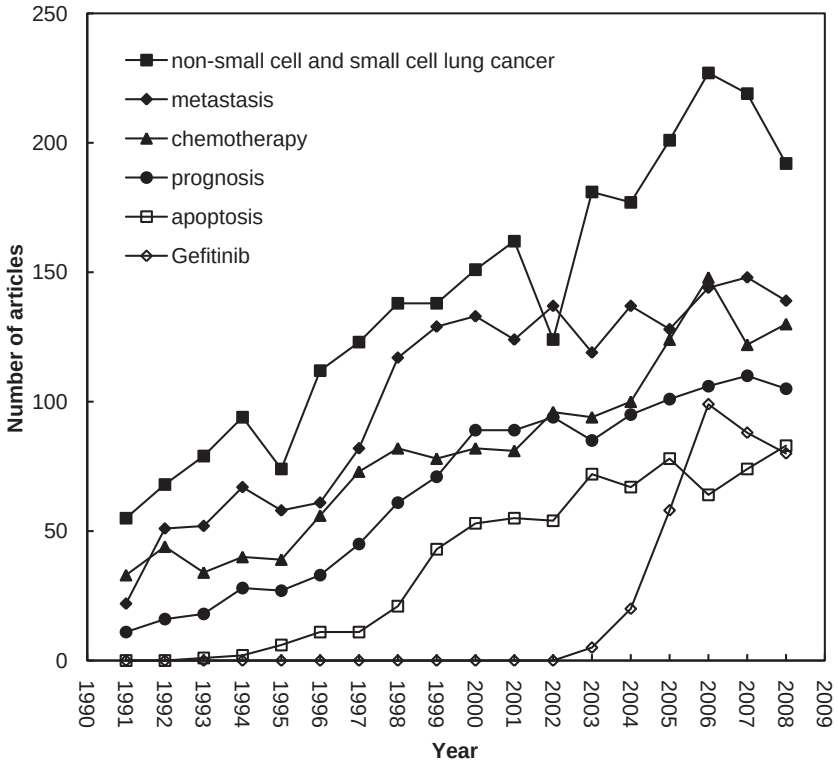

Figure 5. **Growth trends of hotspots in lung cancer related articles, including non-small cell and small cell lung cancer, metastasis, chemotherapy, prognosis, apoptosis, and Gefitinib.**

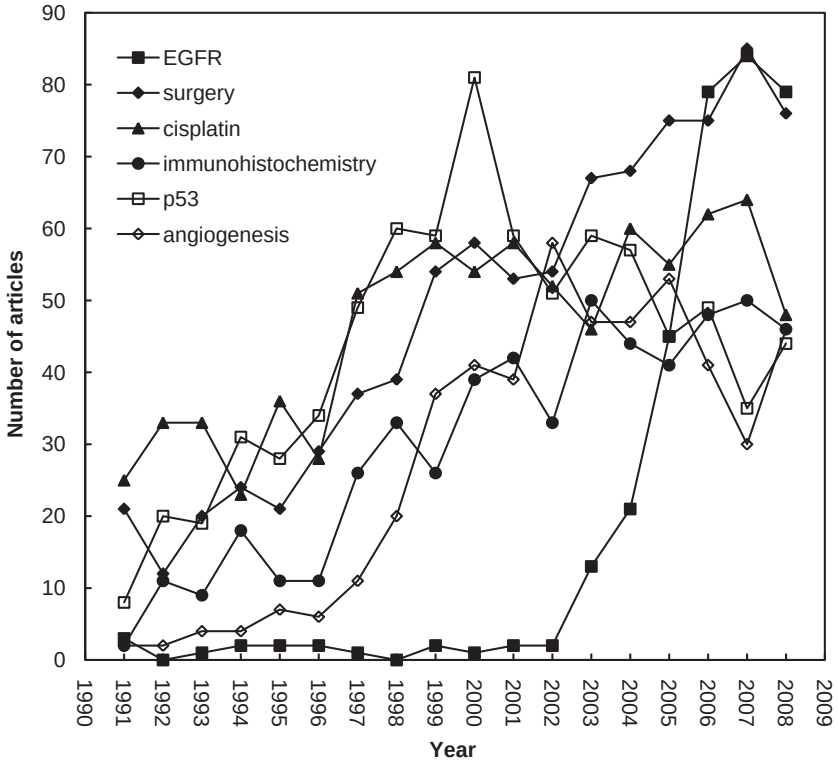

Figure 6. **Growth trends of hotspots in lung cancer related articles, including EGFR, surgery, cisplatin, immunohistochemistry, p53, and angiogenesis.**

search in Japan is still developing, although some research has attained an international level. Participation in the joint clinical studies between many countries is the next issue. Keyword analysis showed that there has been a strategy to connect molecular biology with clinical practice. “Metastasis”, “adenocarcinoma”, and “chemotherapy” were the most popular terms used by Japanese authors. Japan published high impact articles related to non-small cell and small cell

lung cancer. Apoptosis and Gefitinib have been the new research topics in recent years. The findings of this study may be of interest for medical staff who are currently undertaking studies and for those who will be performing research and studying lung cancer medicine for Japanese.

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