

Bibliometrics and visualization analysis of artificial blood vessel research

Li Zhang* and Yakai Feng

The growth and development of research productivity concerning artificial blood vessels in terms of publication output as reflected in Science Citation Index are analysed for the period of 1998–2013 using HistCite to know global publication share, rank, growth rate, citation impact, output of top journals and high-frequency words in this field. The citation chronological chart and main development path are demonstrated by HistCite and Pajek software to understand the basic situation and summarize the research status in the field of artificial blood vessels.

Keywords: Artificial blood vessels, bibliometrics, research output, visualization analysis.

ARTIFICIAL blood vessels are a kind of repairing and replacing diseased vascular prostheses which play an important role in the cardiovascular, reconstructive vascular surgery, tumour and trauma surgery, etc.

Artificial blood vessels are not harvested from natural organ or tissue, but from man-made materials. They can be divided into woven vessels (such as polyethylene terephthalate fibre (Dacron®)^{1,2}, polytetrafluoroethylene (PTFE), silk, etc.) and non-woven vessels (such as expanded PTFE blood vessels, polyurethanes and biodegradable polyester blood vessels, etc.)^{3–6}.

The materials used for artificial blood vessels should have reliable lasting strength and tolerance to different blood flows without deformation and fracture. Furthermore, they must not suffer interference in a complex biochemical environment, and must not cause serious inflammatory or foreign-body reactions. They must be non-carcinogenic *in vivo*, non-toxic, non-teratogenic and have no variation in reactions and not cause various types of allergic diseases. As the human body blood organ, the artificial blood vessels must have good blood and tissue compatibility, and should not cause any destruction of blood components *in vivo*. In addition, they must facilitate surgical sutures, no decoherence in the cut end, and be easy to sterilize and store⁷.

Nowadays, artificial blood vessels have successfully been applied which as prosthetic grafts function satisfactorily only in large-diameter, high-flow vessels. However, in artificial small diameter blood vessels (<6 mm) as prosthetic grafts for coronary arteries, they usually result in early thrombosis, plaque and intimal hyperplasia^{8–10}. Problems such as thrombogenicity, poor vaso-

activity and inappropriate mechanical properties still remain to be solved. Many approaches and strategies have been developed to solve these problems, such as surface biomimetic modification, special morphology, new biomaterials, tissue engineering to prepare the scaffold for artificial blood vessels^{11–14}.

Additionally, the following problems need to be addressed in artificial blood vessels.

- (1) Tissue engineered grafts require an extended period of preparation, so they cannot be used in emergency situations. The prolonged duration of culture increases the risk of infection and raises the cost in terms of manpower, equipment and materials needed¹⁵.
- (2) In order to perfect organ body healing, the endothelial cell should be cultured or sown in advance *in vitro*, so that the artificial blood vessel wall is covered perfectly by endothelial cells before transplantation, thus shortening the time of endothelialization *in vivo* in artificial vessels.
- (3) Enhancing the antibacterial ability to avoid bacterial infection to vascular substitutes.
- (4) Research on new artificial blood vessel materials needs to be explored and strengthened.

Significant advancements in the properties of artificial blood vessels can be expected in the near future with the combination of new biomaterials, tissue engineering and gene therapy. Tissue-engineered blood vessels developed by stem cell technology are suggested to be a promising solution to the above problems^{16,17}.

Scientometrics is a tool by which the state of science and technology can be observed, through the overall production of scientific literature, at a given level of specialization. It provides an approach for assessment of scientific disciplines internationally^{18,19}. Scientometrics

Li Zhang is in the Tianjin University Library, and Yakai Feng is in the School of Chemical Engineering and Technology, Tianjin University, 92 Weijin Road, Tianjin 300072, China.

*For correspondence. (e-mail: zhanglitj@tju.edu.cn)

indicators provide reliable evidence of scientific activity, and have been used in various research topics such as dental science²⁰, psychology^{21,22}, sociology²³, materials science²⁴, hydrogeology²⁵, antioxidants²⁶ and biochemistry, genetics and molecular biology²⁷.

HistCite is an analytical and visual tool which enables analysis of a subject and helps to identify the most significant work on a topic and trace its evolution²⁸.

The present article aims to map artificial blood vessels research as reflected in *Web of Science (WoS)*, by examining the volume of work published in the countries, the journals that publish the research output and their ranking (as reflected by their impact factors) and the high-frequency words, citation situation and main development path using HistCite and Pajek software.

Methodology and source data

All publications on artificial blood vessels were searched with topic of ‘blood vessel prosthesis*’ or ‘artificial blood vessel*’ or ‘vascular graft*’ or ‘vascular prosthesis*’ or ‘artificial vessel*’ from 1998 to 2013 in *Science Citation Index–Expanded (SCIE)*. Then the data on 3643 papers from four document types such as article, proceedings paper, review and meeting abstract were collected.

The data were exported and processed using HistCite to obtain the output of worldwide contributions in the field of artificial blood vessels. The publication year, contribution by countries and journals as well as high-frequency words, highly cited papers, chronological chart and the main development path have been demonstrated and the development status of artificial blood vessels is summarized.

Results and discussion

Year-wise distribution of research output

The number of records obtained from the *SCIE* database for each publication year is given in Figure 1. In 1998, 168 papers on artificial vessels research were published. The growth rate of publication in the following 5 years was slow, but since 2004 the output of papers has been growing steadily.

Global publication share and ranking

Table 1 shows the publication share of the top 10 most productive countries in artificial blood vessels research during 1998–2013. The 16 years from 1998 to 2013 have been divided into three stages: stage 1 from 1998 to 2003; stage 2 from 2004 to 2008; stage 3 from 2009 to 2013. USA tops the list with 1096 papers (30.1%), and paper growth rate from stage 1 to stage 3 is 36.3%. Germany ranks the second, with 9.8% share for 357 papers and growth rate is 57.4%, followed by Japan, China and

France, whose publication shares are 9.0%, 5.9% and 5.6% respectively. China tops the list for paper growth rate from stage 1 to stage 3, indicating that the field has developed very fast during the past 16 years.

Citation-based indicators are valuable and reveal measures of the impact of the scientific work²⁹. Citation analysis is more formal, open, scholarly founded and supplemented in the evaluation of research topic. HistCite also calculates the total local citation score (TLCS) and the total global citation score (TGCS)³⁰. TLCS is the number of times a paper is cited by other papers in the local collection, which means in this study the citation scored by the collection of 3643 papers in the topic of artificial blood vessels. TGCS is the number of times a paper is included in the collection cited in *WoS*.

By comparing citation score per paper among the top 10 countries, it is observed that UK and USA top the list with TLCS per paper of 5.87 and 4.77 and TGCS per paper of 22.96 and 24.55 respectively. This indicates that papers from these countries are cited more by the peer authors in the area of artificial blood vessels and other researchers in *WoS* (Table 2).

Journal-wise distribution of research output

The total number of journals in the collection is 777. The 10 most productive journals published 988 papers in the area of artificial blood vessels, which contributed to 27.12% of the total output of papers during 1998–2013 (Table 3). *Biomaterials* published the higher number of papers (210) in artificial blood vessels during 1998–2013, sharing 5.8% of the total output. The IF-5 of this journal is 8.415 and ranks Q1/Q1 in the corresponding categories of engineering, biomedical/materials science, biomaterials. This is followed by the *Journal of Vascular Surgery* and *European Journal of Vascular and Endovascular Surgery*, which published 3.7% and 3.1% of the total papers output with IF-5 of 3.315 and 2.936 respectively,

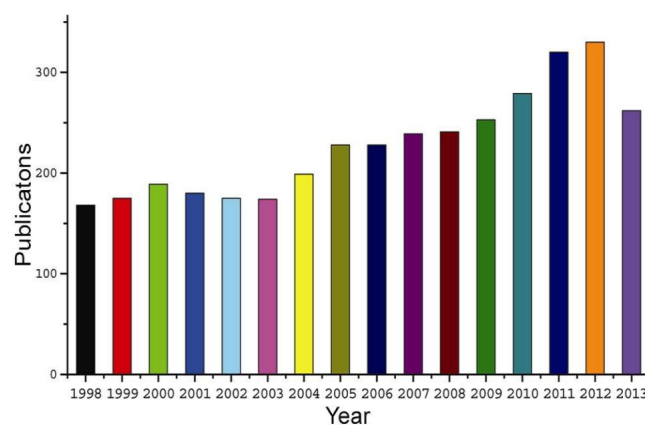


Figure 1. Year-wise publications of artificial blood vessels research output, 1998–2013.

Table 1. Publication output, share and growth rate of top 10 countries in artificial blood vessels research, 1998–2013

| Country | Stage 1 (1998–2003) | Stage 2 (2004–2008) | Stage 3 (2009–2013) | Growth rate from stages 1 to 3 (%) | Total papers | Share (%) |
|-----------------|------------------------|------------------------|------------------------|---------------------------------------|-----------------|--------------|
| USA | 321 | 336 | 439 | 36.3 | 1,096 | 30.1 |
| Germany | 94 | 115 | 148 | 57.4 | 357 | 9.8 |
| Japan | 118 | 96 | 114 | -3.4 | 328 | 9.0 |
| China | 4 | 49 | 163 | 3975 | 216 | 5.9 |
| France | 70 | 63 | 70 | 0 | 203 | 5.6 |
| UK | 69 | 77 | 54 | -21.7 | 200 | 5.5 |
| Italy | 71 | 47 | 69 | -2.8 | 187 | 5.1 |
| The Netherlands | 54 | 48 | 49 | -9.3 | 151 | 4.1 |
| Canada | 38 | 28 | 61 | 60.5 | 127 | 3.5 |
| Switzerland | 20 | 33 | 50 | 150 | 103 | 2.8 |

Table 2. Citation score of top 10 countries in artificial blood vessels research, 1998–2013

| Country | Total papers | TLCS | TLCS/p | TGCS | TGCS/p |
|-----------------|--------------|-------|--------|--------|--------|
| USA | 1,096 | 5,231 | 4.77 | 26,907 | 24.55 |
| Germany | 357 | 903 | 2.53 | 5,200 | 14.57 |
| Japan | 328 | 941 | 2.87 | 3,512 | 10.71 |
| China | 216 | 291 | 1.35 | 1,695 | 7.85 |
| France | 203 | 602 | 2.97 | 2,423 | 11.94 |
| UK | 200 | 1,174 | 5.87 | 4,592 | 22.96 |
| Italy | 187 | 358 | 1.91 | 2,037 | 10.89 |
| The Netherlands | 151 | 637 | 4.22 | 3,182 | 21.07 |
| Canada | 127 | 365 | 2.87 | 2,473 | 19.47 |
| Switzerland | 103 | 392 | 3.81 | 1,395 | 13.54 |

TLCS, Total local citation score; TLCS/p, Total local citation score per paper; TGCS, Total global citation score; TGCS/p, Total global citation score per paper.

and ranked Q2/Q1 in the corresponding categories of peripheral vascular disease/surgery. The *Journal of Biomedical Materials Research, Part A*, which published 2.9% of the total papers, is also remarkable for its high IF-5 of 3.105, ranking Q1/Q2 in engineering, biomedical/materials science, biomaterials categories. From Table 3 the quality of global papers in artificial blood vessels research is noticeable.

Word-wise distribution of research output

Keyword is natural word to express literature theme concept. By analysing changes in keywords, one can grasp the dynamic process, characteristics and rules of the development of the discipline.

‘Vascular’, ‘graft’, ‘tissue’, ‘cells’ and ‘endothelial’ are highest frequency words in the top 50 high-frequency words list of the three stages from 1998 to 2013, which show that cell endothelialization is the research focus in artificial blood vessels. Scientists intend to induce rapid endothelialization on artificial blood vessels to form a stable layer of endothelial³¹. Rapid endothelialization *in situ* can improve the hemocompatibility of the artificial blood vessels and avoid thrombosis^{32,33}. In stage 1 PTFE, Dacron and polyester were the commonly used materials

which appeared in the list from 1998 to 2003, while in stages 2 and 3 (from 2004 to 2013) polyurethane was the preferred material and scaffold technology appeared in artificial blood vessels research. Since 2009, ‘electrospun’ has been the newly involved word in the list in stage 3 and ranked 14th among the top 50 words, revealing that electrospinning technology has been recently introduced in producing artificial blood vessels. This technology enables synthetic polymers and natural polymers to form nanofibrous tubular grafts with various diameters and lengths. The electrospun artificial blood vessels are able to promote cell proliferation, and are becoming a promising substitute for tissue engineering vascular grafts³⁴.

Citation visualization analysis and main development path

HistCite is used to generate the visualized citation chronological chart for papers on artificial blood vessels. A total of 3643 papers were input into HistCite and the top 30 papers with LCS citation were selected to make citation chronological chart (Figure 2). In Figure 2, there are 30 nodes, 63 links; minimum LCS is 46, maximum LCS is 257.

Table 3. Research output and impact factor of top 10 most productive journals contributing to artificial blood vessels, 1998–2013

| Journal | Total papers | Share (%) | IF-5* | Quartile in category** |
|---|--------------|-----------|-------|---|
| <i>Biomaterials</i> | 210 | 5.8 | 8.415 | Q1/Q1 (engineering, biomedical/materials science, biomaterials) |
| <i>Journal of Vascular Surgery</i> | 134 | 3.7 | 3.315 | Q2/Q1 (peripheral vascular disease/surgery) |
| <i>European Journal of Vascular and Endovascular Surgery</i> | 113 | 3.1 | 2.936 | Q2/Q1 (peripheral vascular disease/surgery) |
| <i>Journal of Biomedical Materials Research, Part A</i> | 106 | 2.9 | 3.105 | Q1/Q2 (engineering, biomedical/materials science, biomaterials) |
| <i>Journal of Cardiovascular Surgery</i> | 94 | 2.6 | 1.296 | Q3/Q3/Q2 (cardiac and cardiovascular systems/peripheral vascular disease/surgery) |
| <i>Texas Heart Institute Journal</i> | 94 | 2.6 | 0.747 | Q4 (cardiac and cardiovascular systems) |
| <i>International Journal of Artificial Organs</i> | 67 | 1.8 | 1.540 | Q2/Q3 (engineering, biomedical/transplantation) |
| <i>Journal of Biomedical Materials Research Part B – Applied Biomaterials</i> | 58 | 1.6 | 2.305 | Q2/Q3 (engineering, biomedical/materials science, biomaterials) |
| <i>Annals of Thoracic Surgery</i> | 56 | 1.5 | 3.664 | Q2/Q1/Q1 (cardiac and cardiovascular systems/respiratory system/surgery) |
| <i>Tissue Engineering Part A</i> | 56 | 1.5 | – | – |
| Total | 3,643 | 100 | | |

*Data from JCR 5-year journal impact factor from 2006 to 2010. **Data from JCR journal ranking of quartile in different categories.

Table 4. Top 50 keywords frequency order of artificial blood vessels research output in three stages, 1998–2013

| Stage 1 (1998–2003) | | Stage 2 (2004–2008) | | Stage 3 (2009–2013) | |
|----------------------------|-----------------|---------------------|--------------------|---------------------|--------------------|
| 1 Vascular | 26 Human | 1 Vascular | 26 Endovascular | 1 Vascular | 26 Polyurethane |
| 2 Graft | 27 Model | 2 Graft | 27 Surface | 2 Grafts | 27 Collagen |
| 3 Grafts | 28 Endovascular | 3 Grafts | 28 Vessel | 3 Tissue | 28 Treatment |
| 4 Endothelial | 29 Dacron | 4 Tissue | 29 Novel | 4 Graft | 29 Surface |
| 5 Aortic | 30 Aorta | 5 Cells | 30 Surgery | 5 Cell | 30 Mechanical |
| 6 Cell | 31 Diameter | 6 Endothelial | 31 New | 6 Cells | 31 Prostheses |
| 7 Cells | 32 Engineering | 7 Aortic | 32 Prosthetic | 7 Endothelial | 32 Muscle |
| 8 Tissue | 33 Synthetic | 8 Small | 33 Transplantation | 8 Engineering | 33 Vein |
| 9 Arterial | 34 New | 9 Engineering | 34 Development | 9 Small | 34 Vitro |
| 10 Treatment | 35 Aneurysms | 10 Cell | 35 Evaluation | 10 Aortic | 35 Properties |
| 11 Infection | 36 Using | 11 Blood | 36 Use | 11 Engineered | 36 Use |
| 12 Prostheses | 37 Collagen | 12 Engineered | 37 Repair | 12 Blood | 37 Arterial |
| 13 Blood | 38 Use | 13 Diameter | 38 Poly | 13 Diameter | 38 Heparin |
| 14 Flow | 39 Vivo | 14 Prosthesis | 39 Scaffold | 14 Electrospun | 39 Prosthesis |
| 15 Vitro | 40 Muscle | 15 Infection | 40 Vein | 15 Scaffolds | 40 Transplantation |
| 16 Small | 41 Polyester | 16 Using | 41 Synthetic | 16 Using | 41 Bypass |
| 17 Bypass | 42 Surface | 17 Human | 42 Muscle | 17 Model | 42 Novel |
| 18 Prosthetic | 43 Adhesion | 18 Aneurysm | 43 Patients | 18 Poly | 43 Results |
| 19 Repair | 44 Case | 19 Model | 44 Polyurethane | 19 Human | 44 Surgery |
| 20 Abdominal | 45 Engineered | 20 Vitro | 45 Applications | 20 Based | 45 Term |
| 21 Artery | 46 Expanded | 21 Artery | 46 Collagen | 21 Scaffold | 46 Tubular |
| 22 Evaluation | 47 Experimental | 22 Treatment | 47 EPTFE | 22 Artery | 47 Vessel |
| 23 Aneurysm | 48 Report | 23 Vivo | 48 Results | 23 Infection | 48 Smooth |
| 24 Polytetrafluoroethylene | 49 Surgical | 24 Bypass | 49 Scaffolds | 24 Vivo | 49 Development |
| 25 Prosthesis | 50 Coated | 25 Prostheses | 50 Biodegradable | 25 Stem | 50 Reconstruction |

The size of the box in Figure 2 represents the cited number of papers and the arrows point to the papers which are cited. Figure 2 also shows that research work in artificial blood vessels developed rapidly and actively from 1999 to 2006 and there were several highly cited papers which cited each other during this period. Citation chronological chart reflects the annual change trend, evolution and inheritance relation of research papers in artificial blood vessels.

Interestingly, though paper no. 54, 46 and 101 were published in 1998, paper no. 236 (which was published in 1999) received the highest number of citations, LCS of 257 and GCS of 907 (Figure 2). Paper no. 236 was published in *Science*, in which the authors Niklason *et al.* developed a tissue engineering approach ‘to produce arbitrary lengths of vascular graft material from smooth muscle and endothelial cells that were derived from a biopsy of vascular tissue. Bovine vessels cultured under pulsatile

Table 5. Top 10 high LCS papers on artificial blood vessels, 1998–2013

| Paper no. | Author/title/journal | LCS | LCSx | GCS |
|-----------|--|-----|------|-----|
| 236 | Niklason, L. E. <i>et al.</i> , Functional arteries grown <i>in vitro</i> . <i>Science</i> , 1999, 284 (5413), 489–493. | 257 | 236 | 907 |
| 671 | Kaushal, S., <i>et al.</i> , Functional small-diameter neovessels created using endothelial progenitor cells expanded <i>ex vivo</i> . <i>Nature Med.</i> , 2001, 7 (9), 1035–1040. | 134 | 125 | 457 |
| 1532 | Isenberg, B. C. <i>et al.</i> , Small-diameter artificial arteries engineered <i>in vitro</i> . <i>Circ. Res.</i> , 2006, 98 (1), 25–35. | 93 | 89 | 210 |
| 1389 | Kannan, R. Y. <i>et al.</i> , Current status of prosthetic bypass grafts: a review. <i>J. Biomed. Mater. Res. Part B – Appl. Biomater.</i> , 2005, 74B (1), 570–581. | 86 | 75 | 155 |
| 918 | Xue, L. and Greisler, H. P., Biomaterials in the development and future of vascular grafts. <i>J. Vasc. Surg.</i> , 2003, 37 (2), 472–480. | 84 | 83 | 176 |
| 321 | Deutsch, M. <i>et al.</i> , Clinical autologous <i>in vitro</i> endothelialization of infrainguinal ePTFE grafts in 100 patients: a 9-year experience. <i>Surgery</i> , 1999, 126 (5), 847–855. | 83 | 79 | 160 |
| 555 | Salacinski, H. J. <i>et al.</i> , The mechanical behaviour of vascular grafts: a review. <i>J. Biomater. Appl.</i> , 2001, 15 (3), 241–278. | 80 | 66 | 138 |
| 602 | Meinhart, J. G. <i>et al.</i> , Clinical autologous <i>in vitro</i> endothelialization of 153 infrainguinal ePTFE grafts. <i>Ann. Thorac. Surg.</i> , 2001, 71 (5), S327–S331. | 75 | 72 | 132 |
| 641 | Hoerstrup, S. P. <i>et al.</i> , Tissue engineering of small caliber vascular grafts. <i>Eur. J. Cardio-Thorac. Surg.</i> , 2001, 20 (1), 164–169. | 72 | 68 | 148 |
| 318 | Huynh, T. <i>et al.</i> , Remodeling of an acellular collagen graft into a physiologically responsive neovessel. <i>Nature Biotechnol.</i> , 1999, 17 (11), 1083–1086. | 70 | 70 | 171 |

LCS, Local citation score; LCSx, Local citation score, excluding self-citations; GCS, Global citation score.

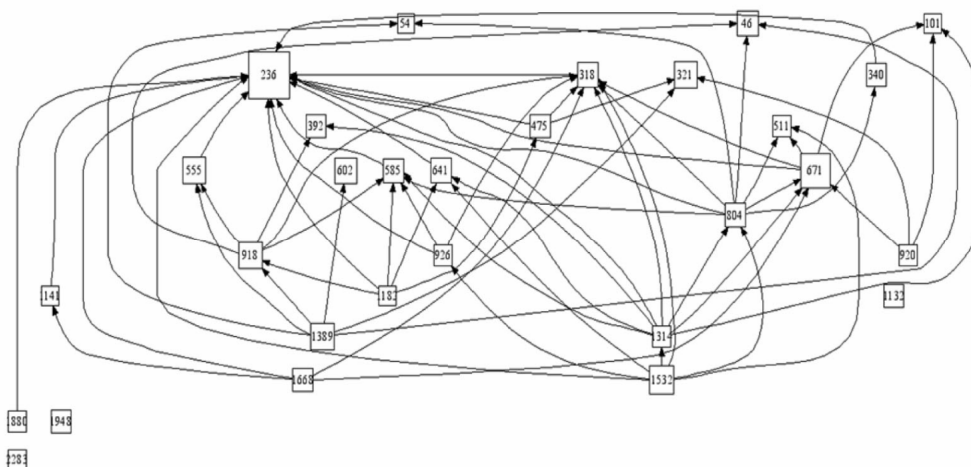


Figure 2. Citation chronological chart for papers of artificial blood vessels.

conditions had rupture strengths greater than 2000 millimeters of mercury, suture retention strengths of up to 90 grams, and collagen contents of up to 50 per cent. Cultured vessels also showed contractile responses to pharmacological agents and contained smooth muscle cells that displayed markers of differentiation such as calponin and myosin heavy chains. Tissue-engineered arteries were implanted in miniature swine, with patency documented up to 24 days by digital angiography³⁵.

Table 5 lists the top 10 high LCS papers on artificial blood vessels from HistCite. These are the important papers in the development of artificial blood vessels in recent years.

The data on LCS top 30 papers were transformed into .net file and input into Pajek to make the main development path map (Figure 3). The nodes represent paper record number, author and year. The direction of the arrow points to the paper which is cited. The path covers 9 years from 1998 to 2006 and 8 papers were involved starting with paper no. 101 (Evidence for circulating bone marrow-derived endothelial cells, 1998), paper no. 236 (Functional arteries grown *in vitro*, 1999), paper no. 318 (Remodeling of an acellular collagen graft into a physiologically responsive neovessel, 1999) and paper no. 511 (Acellular vascular tissues: natural biomaterials for tissue repair and tissue engineering, 2000), which are the

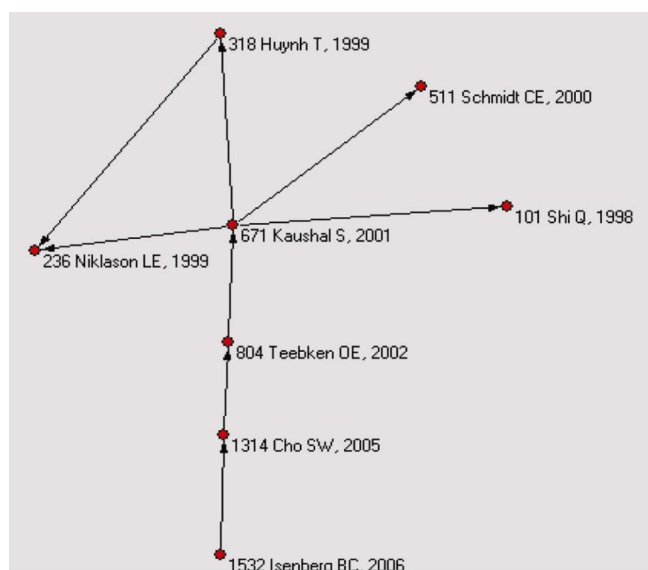


Figure 3. Main development path map for the development of artificial blood vessels.

elementary papers in artificial blood vessels. Paper no. 671 integrated the above four papers and developed functional small-diameter neovessels using endothelial progenitor cells. Later, paper no. 804 reviewed ‘Tissue engineering of small diameter vascular grafts’ in 2002 based on paper no. 671, and then paper no. 1314 developed ‘Small-diameter blood vessels engineered with bone marrow-derived cells’ in 2005 and paper no. 1532 reviewed ‘Small-diameter artificial arteries engineered *in vitro*’ in 2006. The literature in the main path does not include the most cited papers in this field, but puts forward the important theory and innovation concept and represents the main research direction of artificial blood vessels in recent years.

Conclusion

The HistCite-based analysis of artificial blood vessels research has shown how the field has developed in the past 16 years.

The research on artificial blood vessels developed relatively slowly from 1998 to 2003, but since 2004 the output of papers is growing steadily. USA tops the list with 30.1% papers and Germany ranks second (9.8%). China tops the paper growth rate by 3975% from stage 1 to stage 3. Citation score per paper indicates that papers from UK and USA were more cited by peer authors in the area of artificial blood vessels as well as other researchers in *WoS*. The most productive journals publishing artificial blood vessels papers are *Biomaterials* (IF-5 8.415), *Journal of Vascular Surgery* (IF-5 3.315), *European Journal of Vascular and Endovascular Surgery* (IF-5 2.936) and *Journal of Biomedical Materials Research, Part A* (IF-5

3.105), all ranking Q1/Q2 in the corresponding categories.

‘Vascular’, ‘graft’, ‘tissue’, ‘cells’ and ‘endothelial’ are the high-frequency words. Polytetrafluoroethylene, Dacron and polyester were the commonly used materials in the early stage, but from 2004 to 2013 polyurethane has been the preferred material and scaffold technology appeared in artificial blood vessels. ‘Electrospun’ has been the newly involved word since 2009, revealing that electrospinning technology has been recently introduced in producing artificial blood vessels.

HistCite can be used to generate the visualized citation chronological chart for papers on artificial blood vessels. The main path graph obtained using Pajek can determine the most important papers in the stream of citations, which can reveal the development in the area of artificial blood vessels in recent years, i.e. from growing arteries *in vitro* and applying natural biomaterials as acellular vascular tissues to developing small-diameter neovessels and artificial arteries by tissue engineering with cells.

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3. Nerem, R. M. and Seliktar, D., Vascular tissue engineering. *Annu. Rev. Biomed. Eng.*, 2001, **3**, 225–243.
4. Uttayarat, P. *et al.*, Micropatterning of three-dimensional electrospun polyurethane vascular grafts. *Acta Biomater.*, 2010, **6**(11), 4229–4237.
5. Bergmeister, H. *et al.*, Electrospun small-diameter polyurethane vascular grafts: ingrowth and differentiation of vascular-specific host cells. *Artif. Organs*, 2012, **36**(1), 54–61.
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21. Barrios, M., Villarroja, A. and Borrego, A., Scientific production in psychology: a gender analysis. *Scientometrics*, 2013, **95**(1), 15–23.
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ACKNOWLEDGEMENTS. This project was supported by the National Natural Science Foundation of China (Grant No. 31370969), and the International Cooperation from the Ministry of Science and Technology of China (Grant No. 2013DFG52040).

Received 4 February 2014; revised accepted 10 February 2014