Plastic Surgery and Acellular Dermal Matrix: Highlighting Trends from 1999 to 2013

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ABSTRACT
The last decade has ushered in a rapidly expanding global discussion regarding acellular dermal matrix (ADM) applications, economic analyses, technical considerations, benefits, and risks, with recent emphasis on ADM use in breast surgery. This study aims to evaluate global trends in ADM research using bibliometric analysis. The top nine Plastic Surgery journals were determined by impact factor (IF). Each issue of the nine journals between 1999 and 2013 was accessed to compile a database of articles discussing ADM. Publications were further classified by IF, authors’ geographic location, study design, and level of evidence (LOE, I-V). Productivity index and productivity share were calculated for each region. In total, 256 ADM articles were accessed. The annual global publication volume increased significantly by 4.2 (0.87) articles per year (p<0.001), with a mean productivity index of 36.3 (59.0). The mean impact factor of the nine journals increased significantly from 0.61 (0.11) to 2.47 (0.99) from 1993 to 2013 (p<0.001). Despite this increase in the global ADM literature, the majority of research was of weaker LOE (level I: 2.29% and level II: 9.17%). USA contributed the most research (87%), followed by Asia (4.76%) and Western Europe (4.71%). USA contributed the greatest volume of research. Regarding clinical application of ADM, the majority of publications focused on ADM use in breast surgery, specifically breast reconstruction (154 articles, 60.2%). The majority of research was of lower LOE; thus, efforts should be made to strengthen the body of literature, particularly with regard to cost analysis.

KEYWORDS
Bibliometrics; Acellular dermal matrix; Trends; Global

INTRODUCTION
Acellular dermal matrices (ADM) were first introduced clinically in reconstructive surgery in 1994 in the context of burn therapy and have since become widely used in reconstruction of chronic wounds, breast, and abdominal wall defects.1-3 ADMs are created through a process of decellularization, while the extracellular matrix is left intact. The matrix then acts as a tissue graft upon
which the patient’s own cells can recolonize and vascularize. Their role as a biologic material is to provide structural integrity and serve as a scaffold for vascular and tissue ingrowth. Since the advent of clinical ADM use, numerous applications and products have come to market, bolstering the armamentarium of the reconstructive surgeon. Given its significant added cost, the surgical community has turned to cost-benefit analysis to justify its use.

As evidence-based medicine becomes increasingly influential in formulating health policy and reimbursement, effort has been put forth to increase the volume and quality of research in the Plastic Surgery literature, especially for new or experimental technologies and methodologies. Specifically, recent advances in breast surgery have focused on the use of ADM in post-mastectomy reconstruction, as well as to a lesser extent cosmetic and revision surgeries. A common hurdle in breast reconstruction is the need to obtain adequate vascularized soft tissue in order to cover the breast implant while still allowing sufficient blood supply. ADM has mitigated some of these potential complications by equipping surgeons with the ability to achieve adequate vascularization of tissue through an alternative means. Initial studies by Breuing et al. (2005) and Bindingnavele et al. (2007) reported the use of ADM in implant-based breast and tissue expander-based reconstructions, respectively. These initial studies prompted an influx of subsequent reports addressing the concept of ADM use for breast reconstruction with post-operative radiation, as well as complication rates with ADM in various breast reconstruction modalities. With this recent increase in application, there is a need for better ways for surgeons to evaluate the current clinical picture and trends in ADM research to make more informed decisions and guide future research. To our knowledge, no other groups have studied this important area of inquiry.

To reach these ends, the present study utilizes bibliometry, which is a method of providing quantitative analysis of literature to extrapolate productivity and trends. Assessment of both quantity and quality of the existing academic literature in a particular field of study facilitates an objective determination of a specific publication’s impact or contribution to that body of literature. This method has been used in various medical and academic fields, e.g., hand surgery, rehabilitation, public health, and environmental assessment. Variables central to bibliometric analysis include impact factor (IF) and level of evidence (LOE) in addition to research productivity and publication volume. The IF is calculated by dividing the number of citations credited to a journal over a two-year period by the number of articles published by that journal during the timeframe. It is regarded as a credible means of assessing the relative influence of a journal in a particular field of study.

Of similar importance is LOE, which classifies articles on a I-V scale according to the research methodology used within the study. LOE assignment has gained popularity in Plastic Surgery literature, with major journals such as *Plastic and Reconstructive Surgery* and *Aesthetic Surgery Journal* providing a classification for each article published by the journal. In turn, as popularity in clinical use of ADM has continued to climb over the past 20 years, assessing key publication trends in LOE and IF in ADM literature can provide an insightful look into the relationship between research and medical technology adoption and practice.

This study evaluates the global trends in ADM research using bibliometric analysis in order to explore the relationship between research and clinical practice, as well as interpret how these trends shape global discussion and use of technology.

**MATERIALS AND METHODS**

**Data Collection**

The top English-language Plastic Surgery journals (n=9) were selected based on 2013 impact factor (IF), as determined by the Journal Citation Reports of the Institution for Scientific Information. Only those journals which published on ADM were included. Next, the ADM manuscripts of each issue of the 9 journals between 1999 and 2013 as determined by the earliest ADM publication date were accessed directly, either in-print or electronically. Each article was classified by journal, year of publication, title, IF, author’s geographic location, study design, and LOE.

**Journal and Article Selection Criteria**

The following journals were investigated:

- *Aesthetic Plastic Surgery*
- *Aesthetic Surgery*
Journal; Annals of Plastic Surgery; The Canadian Journal of Plastic Surgery (now Plastic Surgery); Clinics in Plastic Surgery; Journal of Plastic, Reconstructive and Aesthetic Surgery (previously known as British Journal of Plastic Surgery); Journal of Plastic Surgery and Hand Surgery (previously known as Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery); Journal of Reconstructive Microsurgery; and Plastic and Reconstructive Surgery. All original peer-reviewed articles regarding acellular dermal matrix were analyzed. Case reports, reports on technique, and literature reviews were included, while editorials and letters, book reviews, and conference abstracts were excluded. Articles with significant overlap to previous studies, possibly in other journals, were excluded to prevent duplication of numbers.

Impact Factor
An impact factor was assigned to each article based on the IF its journal received for the given year it was published, as issued by the Journal Citation Reports of the Institution for Scientific Information. The use of IF varied among the journals; therefore articles were excluded if a journal was not assigned an IF for that corresponding year. Table 1 shows IF inception for each given journal, the number of publications excluded due to lack of IF, and the total number of publications included.

Authors’ Geographic Region
Each article was assigned a geographic region and country based on the composition of contributing authors and their affiliated institutions. The nine geographic regions, which have been defined in previously published studies, are based on scientific, geographic, and economic measures: Africa, Asia (excluding Japan), Canada, Eastern Europe (including all formerly socialist economies of Europe), Western Europe (including the remainder of Europe plus Greenland), Japan, Latin America (including the Caribbean), Oceania (including Australia, New Zealand, and New Guinea), and USA. If multiple regions were represented, each was weighted by the proportion of authors from that region.

Study Design
Publications were determined to be either clinically focused or basic science in nature. Clinical studies were further defined as diagnostic, therapeutic, or prognostic. Basic science studies were defined as animal, cadaveric, histologic, or protein.

Level of Evidence
Level of evidence was determined by using the study authors’ self-reported assignment or when not available was assigned according to the American Society of Plastic Surgery level of evidence pyramid guideline. All clinical research articles received a I-V LOE assignment, while basic science articles were considered separately.

Productivity Index
Similar to previously published bibliometric

Table 1: Impact factor inception varied among the various journals. Publications were excluded if the respective journal was not assigned an impact factor for that given year. In total, 15 articles were excluded due to this discrepancy yielding a total of 256 articles in the database.

<table>
<thead>
<tr>
<th>Journal</th>
<th>Impact Factor Inception (Year)</th>
<th>Publications Excluded</th>
<th>Publications Included</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aesthetic Plastic Surgery</td>
<td>1992*</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Aesthetic Surgery Journal</td>
<td>2011</td>
<td>11</td>
<td>21</td>
</tr>
<tr>
<td>Annals of Plastic Surgery</td>
<td>1992*</td>
<td>0</td>
<td>63</td>
</tr>
<tr>
<td>Canadian Journal of Plastic Surgery</td>
<td>2010</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Clinics in Plastic Surgery</td>
<td>1992*</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>Journal of Plastic, Reconstructive, and Aesthetic Surgery</td>
<td>2007</td>
<td>1</td>
<td>24</td>
</tr>
<tr>
<td>Journal of Plastic Surgery and Hand Surgery</td>
<td>1997</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Journal of Reconstructive Microsurgery</td>
<td>1992*</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Plastic and Reconstructive Surgery</td>
<td>1992*</td>
<td>0</td>
<td>113</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>15</td>
<td>256</td>
</tr>
</tbody>
</table>

*Earliest record of IFs online started in 1992.
studies, productivity index was defined as the number of articles published in a journal by a given region multiplied by the journal’s impact factor for each article’s corresponding year.\textsuperscript{26-28}

\textit{Productivity Share}

To objectively compare the degree to which different geographic regions contributed to the ADM literature over the observed time period, productivity share was calculated for each region. Using 5-year simple moving averages, the total global productivity index calculated for a given 5-year period was divided by the average productivity index contributed by a region. Thus from 1999-2013 there were 11 consecutive overlapping 5-year periods observed (e.g., 1999-2003, 2000-2004, etc.). Productivity share by country was also calculated.

\textit{Areas of Interest for ADM Use}

Articles queried from the dataset were analyzed for specific area of interest in which ADM was used, including abdomen, breast, burn and skin, chest, extremities, face/head and neck, and other areas. Use of ADM in breast surgery was specifically highlighted in this study, and the dataset was further analyzed for specific application in which ADM was used in breast surgery including: reconstruction, revision surgery, cosmetic, general breast surgery (including some or all of the previously mentioned types of breast surgery) or none of the above (typically basic science articles).

\textit{Statistical Analysis}

Statistical comparisons were achieved using univariate linear regression with time as the independent variable and number of articles, productivity index, or productivity share being the dependent variable. Statistical significance was defined as \( p<0.05 \). When necessary, statistics were reported as mean (SD). All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY).

\textbf{RESULTS}

\textbf{Journal and Article Selection Criteria}

Over the 15-year period lasting from 1999 to 2013, a total of 256 articles regarding ADM were published in the 9 journals studied. The annual global volume of publications increased significantly by 4.2±0.87 articles per year (\( N=256, p<0.001, R^2=0.64 \)) (Figure 1). \textit{Plastic and Reconstructive Surgery} contained the most ADM-related publications with 113 articles (44.1%), followed by

\textbf{Fig. 1: Volume and productivity of acellular dermal matrix research from 1999 to 2013 (N = 256)}

The blue solid line denotes the volume of research published. Among the top 9 Plastic Surgery journals by impact factor during the study period, the annual global volume of publications increased significantly by 4.2±0.87 articles per year (\( N=256, p<0.001 \)). The red dashed line depicts productivity index over time, which was defined as the number of articles published in a journal by a given region multiplied by the journal’s impact factor for each article’s corresponding year. Global productivity index also demonstrated a significant increase of 10.2±2.3 per year (\( p=0.001 \)).
Journal of Plastic, Reconstructive, and Aesthetic Surgery (63 articles, 24.6%) and Annals of Plastic Surgery (24 articles, 9.4%) (Figure 2). These three were the only journals to experience a significant increase in publication volume over the 15-year period ($p=0.001$, $R^2=0.58$; $p<0.001$, $R^2=0.66$; and $p=0.002$, $R^2=0.53$, respectively).

Impact Factor

A total of 15 publications were removed due to lack of available journal impact factor for their given year (Table 1). From 1999-2013 the mean impact factor of the 9 journals increased significantly from 0.61 (0.11) in 1999 to 2.47 (0.99) in 2013 ($p<0.001$, $R^2=0.67$) (Figure 3).

Fig. 2: Total number of articles on acellular dermal matrix published in the top 9 Plastic Surgery journals by impact factor from 1999 to 2013, for years when journal impact factor data was available. Plastic and Reconstructive Surgery published most frequently with 113 articles (44.1%), followed by Annals of Plastic Surgery (63 articles, 24.6%) and Journal of Plastic, Reconstructive, and Aesthetic Surgery (24 articles, 9.4%).

Fig. 3: From 1999-2013, the mean impact factor for the top 9 Plastic Surgery journals by impact factor representing respective articles in our study sample increased significantly from 0.61 in 1999 to 2.47 in 2013 ($p<0.001$).
**Study Design**

The majority of research during the study period was classified as clinical (218 articles, 85.2%), while the minority was basic science in nature (38 articles, 14.8%). The USA produced the highest volume of basic science research with 28 published articles (73.7%) over the study period. Nearly all of the clinical studies (212 articles, 97.3%) evaluated therapeutic interventions, while the remainder (6 articles, 2.7%) were prognostic.

**Level of Evidence**

In the publication sample, 85.5% of the articles were non-randomized controlled trials (LOE III, IV, or V). There were 5 (2.3%) level I studies, 20 (9.2%) level II studies, 52 (23.9%) level III studies, 71 (32.6%) level IV studies, and 70 (32.1%) level V studies. Univariate linear regression analysis demonstrated a statistically significant increase in number of publications at all levels of evidence over the 15-year period \( (p=0.02, R^2=0.34; p=0.01, R^2=0.39; p=0.001, R^2=0.55; p<0.001, R^2=0.77; \) and \( p=0.006, R^2=0.45, \) respectively). In concordance with the large jump in publication volume beginning in 2011, there was also a large increase in level III through V studies (Figure 4).

**Productivity Index**

The total global research productivity index in ADM was 544.5, with a mean productivity index over the 15-year period of 36.3 (59.0) and a significant increase of 10.2 (2.3) per year \( (p=0.001, R^2=0.59) \) (Figure 1). By geographic region, the USA demonstrated the largest productivity index, contributing 87.4%. Asia added 4.8% to the global total, while Western Europe (4.7%), Canada (2.3%), Japan (0.49%), and Latin America (0.37%) contributed to a lesser degree (Figure 5).

**Productivity Share**

As a proportion of the global contribution to the ADM literature, the USA consistently had the greatest productivity share of all regions analyzed [mean (SD), 89.1% (7.6%)] during the 15-year study period (Figure 6). While the USA maintained the majority among all the regions studied in productivity share, those that had significant increases in productivity share over the 15-year period were Western Europe,
Fig. 5: Productivity index in acellular dermal matrix by geographic region. During the study period from 1999 to 2013, the USA demonstrated the largest productivity index, contributing 87.4%. Asia contributed 4.8% of the global total, while Western Europe (4.7%), Canada (2.3%), Japan (0.49%), and Latin America (0.37%) contributed a smaller proportion of overall global productivity.

Fig. 6: Changes in acellular dermal matrix research productivity between geographic regions over 1999 to 2013. Productivity share was defined as the total global productivity index calculated for a given 5-year period divided by the average productivity index contributed by a region. USA supplied the greatest productivity share of the total global contribution to ADM literature generated each year during the 15-year study period (mean 89.1±7.6%). While the USA maintained the majority among all the regions studied in productivity share, those that had significant increases in productivity share over the 15-year period were Western Europe, Canada, and Asia.
Canada, and Asia. Changes in productivity share over time were also evaluated for individual countries. When broken down by country, Austria ($p=0.031$, $R^2=0.42$), Canada ($p=0.006$, $R^2=0.59$), Spain ($p=0.01$, $R^2=0.54$), Taiwan ($p=0.029$, $R^2=0.43$), Turkey ($p=0.03$, $R^2=0.42$), and UK ($p=0.036$, $R^2=0.40$) experienced significant increases. No country experienced a significant decrease in productivity share.

Areas of Interest for ADM Use

Further segregation of the ADM literature by special interest topic reveals that publications related to the use of ADM in breast surgery represent the majority (154 articles, 60.2%), followed by abdominal reconstruction (33 articles, 12.9%), miscellaneous use (31 articles, 12.1%), face/head and neck reconstruction (20 articles, 7.8%), extremity reconstruction (11 articles, 4.3%), burn reconstruction (4 articles, 1.6%), and chest reconstruction (3 articles, 1.1%) (Figure 7). Further breakdown of breast surgery ADM use highlighted breast reconstruction with ADM as the clear majority (71%), followed by revision surgery (9%) and cosmetic surgery (4%). The remaining articles either studied ADM use in all 3 types of breast surgery (9%) or were non-clinical studies (7%).

DISCUSSION

Since its debut in the early 1990’s, acellular dermal matrix using in Plastic Surgery has expanded to include breast, abdominal wall, chest wall, head and neck, burn, wound and skin reconstruction.1-5 Most recently, the use of ADM in breast reconstruction has gained popularity and accounts for a majority of the publications related to ADM use. As evidence-based medicine continues to be a major focus in determining fair physician reimbursement policies, efforts to objectively assess the quality of the research are crucial. The purpose of this study was to objectively evaluate the global trends in ADM related research over a 15-year period (1999-2013).

In this study, a majority of the papers were related to ADM use in breast surgery, specifically postmastectomy reconstruction (60.2%). Primarily used as an inferior-lateral sling in two-stage breast reconstruction, ADM aids in maintaining control of the inframammary fold, decreasing ptosis, increasing projection, and improving overall implant coverage and tissue revascularization.29-31 Conflicting data regarding post-operative complications of ADM in breast surgery has been published,
however, there continues to be a significant uptick in reconstructive surgery cases mainly due to the US Women’s Health and Cancer Rights Act of 1998.

Since the advent of the US Women’s Health and Cancer Rights Act of 1998, which requires all health insurance companies to provide reimbursement for the reconstruction of both breasts, there has been a dramatic increase in the number of women receiving breast reconstruction following mastectomy.32 The Act effectively established a paradigm shift in reconstructive breast surgery, prompting a surge of new reconstructive cases following mastectomy.23

A well-cited study by Jagsi et al. analyzed breast reconstruction trends over a 10-year period. They discovered that post-mastectomy breast reconstruction rose from 46 percent in 1998 to 63 percent in 2007.33 Furthermore, 76.2 percent of women having bilateral mastectomies opted for reconstruction. According to ASPS, there were 95,589 reconstructive breast procedures performed in the US in 2013—a 4 percent increase from 2012 and a 21 percent increase from 2000.34 This rise in new cases could potentially explain the increased popularity of ADM use and research in the area of breast surgery.

In addition, market data from Life Cell Corporation (Bridgewater, NJ) demonstrates that 87 percent of surgeons who perform at least 25 breast reconstructions per year have used a biologic material in their implant-based reconstructions. Furthermore, over 56 percent of all tissue expander/implant-based reconstructions are now done using biologic mesh.34 Thus, the major increase in ADM publications may be due in part to the fact that women are increasingly seeking reconstruction following mastectomy, a majority of which are completed using ADM.35 Moreover, the increasing use of both skin- and nipple-sparing mastectomy, access to BRCA testing, and improved breast implants accompany the rise in ADM use.36 Each of these trends and enhancements favor the increased use of prosthetic breast reconstruction and as such may contribute to an increase in ADM use. Further investigation into this correlation is warranted.

This study highlights the USA as the largest contributor to the ADM literature in Plastic Surgery. This mirrors the trend of overall publications in Plastic Surgery, as well as with respect to the most highly cited articles in the field.37 The largest increases in global ADM research productivity occurred during 2011 and 2012, with growth in productivity index from 42.2 in 2010 to 86.5 in 2011, and up to 194.2 in 2012. Increased interest in breast reconstruction following passage of the 2008 Women’s Health and Cancer Rights Act as well as improved insurance reimbursement for ADM are largely responsible for this period of growth. For example, in 2008, Kinetic Concepts, Inc. (KCI, San Antonio, TX) acquired major allograft producer, Life Cell (Bridgewater, NJ), and in that same year released Strattice (Life Cell, Bridgewater, NJ), an acellular reconstructive tissue matrix derived from porcine dermis.38 The company’s efforts to increase reimbursement coverage were successful in subsequent years.39-40 Reimbursement coverage evolves in parallel with peer-reviewed clinical evidence demonstrating a product’s outcome-related data. KCI (San Antonio, TX) reports that demand for their allograft products correlates with reimbursement rates by 3rd-party payers (e.g., Medicare, Medicaid, etc.).39,40 Thus, the increased publication volume may be the result of expanding product reimbursement, inspiring an increase in ADM use and consequently improved research efforts.

As ADM use becomes increasingly prevalent, further research validating their impact on patient-centered outcomes will be paramount. With the implementation of the Affordable Care Act, the fee-for-service payment model is slowly being replaced by a reimbursement system tied to quality of care standards and cost savings measures.41,42 As new health policy increases patients’ access to oncologic procedures and therefore reconstruction, overall ADM use will increase. Given their significant added cost, it is imperative that the Plastic Surgery literature objectively addresses its impact on patient outcomes.42

The majority of ADM research was shown to be of low LOE (level IV, V), which is consistent with previous studies regarding ADM use in breast reconstruction, as well as with the Plastic Surgery literature in general.43,44 This dearth of randomized-controlled trials has presented a challenge to receiving full advocacy for the product and asserting its benefit within a cost-conscious healthcare structure. In 2013, the ASPS released evidence-based practice guidelines on prosthetic breast reconstruction, citing the use of ADM to have “varied and conflicting”
In conclusion, between 1999 and 2013 there has been significant growth in the volume and impact of acellular dermal matrix research published in the top 9 Plastic Surgery journals as rated by impact factor. Over this 15-year study period, publications on ADM use in breast reconstruction were most prevalent, and the USA was the greatest contributor to ADM research both in terms of publication volume and productivity, with the largest increase in productivity between 2011 and 2012. The majority of publications were of lower LOE, although a there was a significant increase in LOE at all levels. In order to ensure its viability in the armamentarium of the Plastic and Reconstructive Surgeon, future research endeavors to further validate the cost-effectiveness of ADM use must be undertaken.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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