

Trends, Gaps, and Collaboration in Facial Transplantation: A Bibliometric Study

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Background: Facial transplantation (FT) has advanced extensively over the past two decades, with over 40 transplants performed to date. Over this time, the FT literature has evolved as well, from early discussions on ethics and feasibility of FT to functional outcomes reports more recently. We aimed to evaluate the entire body of FT literature to identify trends in publications over time in addition to current existing gaps in the field.

Methods: We conducted a comprehensive bibliometric analysis of the published FT literature from 1994, the first year FT was mentioned in the literature, through July 2020. Co-authorship and keyword information were analyzed using VOSviewer. Articles were manually categorized based on keywords and their aim to provide insight on trends.

Results: A total of 2182 articles were identified. Analysis identified the top 50 publishing authors in the field and demonstrated co-authorship linkage between 84.8% of the top 1000 authors. Clinical surgical techniques, protocols, and experiments were the most frequently published category. Within clinical outcomes, immunologic outcomes were most frequent, while psychosocial were the lowest. Gaps were identified in long-term outcomes reporting and patient-reported outcomes, with physician-reported outcomes heavily outweighing patient-reported outcomes.

Conclusions: As the field continues to evolve, rigorous tracking of publication patterns over time will encourage development of a more robust evidence base, identify gaps in the published literature, and highlight opportunities to enhance collaboration in the field. This data will provide surgeons and research institutions with information to further improve this life-changing procedure. (*Plast Reconstr Surg Glob Open* 2022;10:e4248; doi: [10.1097/GOX.0000000000004248](https://doi.org/10.1097/GOX.0000000000004248); Published online 15 April 2022.)

INTRODUCTION

The concept of facial transplantation (FT) was introduced in the literature as a hypothetical surgical option three decades ago after the first medical conference on composite tissue allotransplantation, hosted by the Rehabilitation Research & Development Service of the United States Department of Veterans Affairs in September 1991.¹ The field quickly moved from theoretical to clinical reality, with close to 50 FTs performed to date in 11 countries.¹ This life-altering procedure, first pioneered in 2005 in Paris with a partial FT, is reserved for

severe facial injuries not amenable to conventional reconstructive procedures.^{2,3}

The rapid growth in clinical experience and interest in FT has resulted in substantial growth in publications. However, the pace of clinical FT developments has exceeded that of the published literature. Additionally, there are delays in publication due to long wait times from submission to publication, taking up to a year or more from the date of transplantation to final publication.⁴ Further deficits in the literature may result from hesitancy to publish complications or suboptimal results. The literature is best analyzed in its entirety, creating an opportunity to analyze the literature and identify gaps and trends.

Subjective evaluation of the field appears to reveal a transition from a focus on ethics to feasibility with animal and cadaveric models, and most recently clinical reports. Despite the significant expansion in knowledge, many questions remain unanswered, including the long-term survival of an allograft and the impact of FT on patients and their QoL. Prior attempts have been made to aggregate data in the form of systematic and qualitative reviews, but these methods have their limitations.⁵ Advanced

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quantitative assessment techniques, such as bibliometric analyses, would benefit the field of FT. Bibliometric analysis proves advantageous by utilizing statistical analysis specifically designed to assess literature and publications: authorship, publication date, networks, and several other factors. The bibliometric tools for data analysis deliver insights into the field’s evolution over time as well. Categorization and mapping of trends over time in the facial transplant literature would allow visualization of progress and the current state of the field.⁶

The purpose of this study was to perform a bibliometric analysis of the spectrum of the FT literature published to date. We hypothesize that the overall publication rates have increased over the past twenty years, there will be a gap in the literature reporting long-term and patient-reported outcomes, and collaboration within the field has room to improve.

METHODS

Search Strategy

Three electronic databases (PubMed, Embase, and SCOPUS) were queried from July 1994 through July 2020. The search terms are shown in Table 1. Articles were exported to EndNoteX9 (Clarivate, Boston, Mass.), duplicates were removed, and articles were evaluated for inclusion (Fig. 1). A total of 2182 articles were included in our analysis. If separate articles reported on the same patient case, they were included individually in the analysis, as opposed to condensing articles into one group per patient.

VOSviewer Data Collection

To analyze the number of publications and connections between authors in the FT literature, we used VOSviewer (version 1.6.15, Centre for Science and Technology Studies, Leiden University, The Netherlands) software to create visual maps depicting co-authorship networks and publication frequency.⁷⁻¹⁰ Fractional counting, which takes into account the number of co-authors, was used to create a more accurate representation of authors’ impact on the literature.⁸ For example, when there were 10 co-authors, an author received one tenth of a link.¹¹ Singular authors often appeared in the literature under more than

Table 1. Systematic Search Strategy

Search Terms Used in Databases
Facial transplantation
Face transplant
Facial transplant
Face transplantation
Face allotransplantation
Facial allotransplantation
Facial vascularized composite allotransplantation
Face vascularized composite allotransplantation
Face allograft
Facial allograft
Face composite tissue allotransplantation
Facial composite tissue allotransplantation
Face composite tissue allograft
Facial composite tissue allograft
Face vascularized composite allograft
Facial vascularized composite allograft

Takeaways

Question: Despite significant advances in FT, quantitative analysis of the field has yet to be performed. We aim to evaluate the entire body of literature to identify trends in publications over time and identify current gaps in the field.

Findings: Two thousand one hundred eighty-two articles have been published on FT, with early publications focused primarily on ethics, with a gradual transition toward increased clinical focus following the first successful transplant in 2005.

Meaning: The FT literature is evolving as both number of transplants and length of follow-up increases; however, with growth in the field comes new challenges.

one name (eg, Rodriguez, e. and Rodriguez, e. d.). The VOSviewer thesaurus tool was used to fix this issue and group one author’s various names under a singular label for accurate bibliometric analysis.¹⁰ Authors with at least five publications were included in our bibliometric analysis. We analyzed the top 50 and 1000 authors to provide a focused view on the most published authors while also analyzing the field at large. We selected 1000 as it is the upper limit for analysis with VOSviewer.

VOSviewer was also used to create a keyword map to highlight the most prevalent keywords. Keywords were quantified with fractional counting and subsequently used to categorize articles. In the maps, the resolution was set to 0.03 to provide the greatest number of clusters that could be visualized at once, and minimum cluster size was set to one.

Categorization

Articles were sorted into three categories: ethics and opinions/editorials (op-eds), preclinical, and clinical.^{12,13} Preclinical included animal/translational models along with cadaveric studies, while clinical included techniques and outcomes of FTs. Subcategories based on keywords from VOSviewer were established, and the articles were sorted. For example, articles were screened in Microsoft Excel (Microsoft Corp, Redmond, Wash.) based on the presence of the keywords like “immunology” and “rejection,” then manually reviewed before being placed in the “immunological outcomes” category. Clinical outcomes were further subcategorized as long and short term, with long-term defined as one year or more posttransplant, a standard timeline in the surgical field.¹⁴ Articles that were relevant to more than one category or subcategory were included in all applicable groups to maximize relative data and generalizability.

Data Analysis

Data analysis was performed in Excel to determine collaboration strength, network links, and category percentages over time. Order two polynomial trendlines were applied to the data and R² values were extracted to provide quantitative evidence that publications were increasing or decreasing over time.

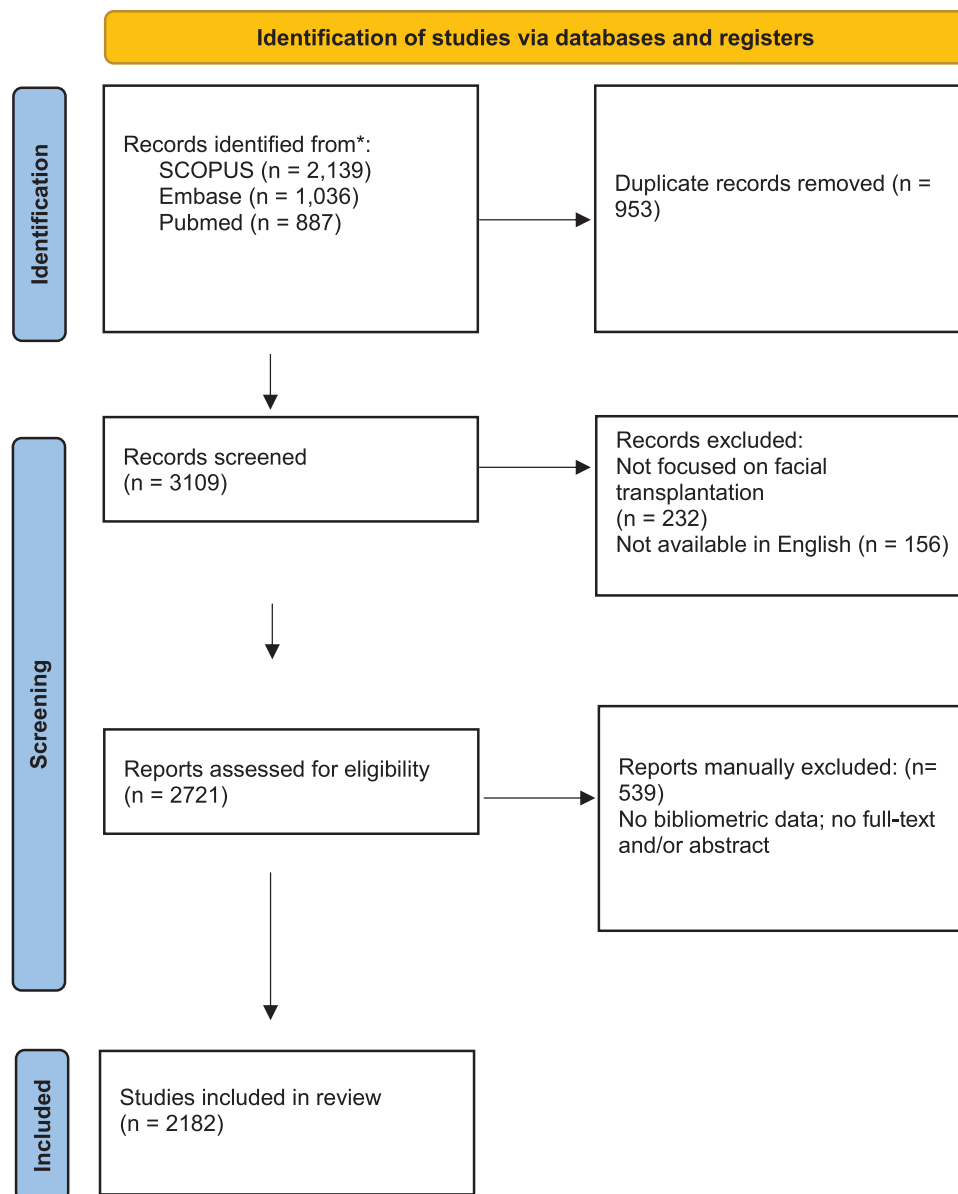


Fig. 1. PRISMA.

RESULTS

VOSviewer

The literature showed high levels of inter-connection between the most published authors, with 86% of the top 50 authors and 84.8% of the top 1000 authors linked by co-authorship. Figure 2 depicts the top 50 authors with their respective clusters, concentrated around the top five authors, along with the co-authorship connections between the clusters.

The top 15 authors, along with their publication frequency are listed in Figure 3. M. Siemionow, B. Pomahac, and E.D. Rodriguez were the top three publishing authors with 203, 177, and 145 articles, respectively. These three authors are all in the United States and have been

involved in at least one FT, with B. Pomahac and E.D. Rodriguez involved in several FTs each. The most published in journal for each of these three authors was *Plastic and Reconstructive Surgery*. Figure 4 depicts the VOSviewer keyword map.

Categorization

The largest category was clinical research with 1163 publications, followed by 605 preclinical publications and 466 ethics/opinions/editorials publications. Further sub-categorization from the highest to lowest number of publications was as follows: surgical techniques, protocols, and clinical experiments; animal and translational models; ethics, opinions, and editorials; outcomes; and cadaveric models (Fig. 5).

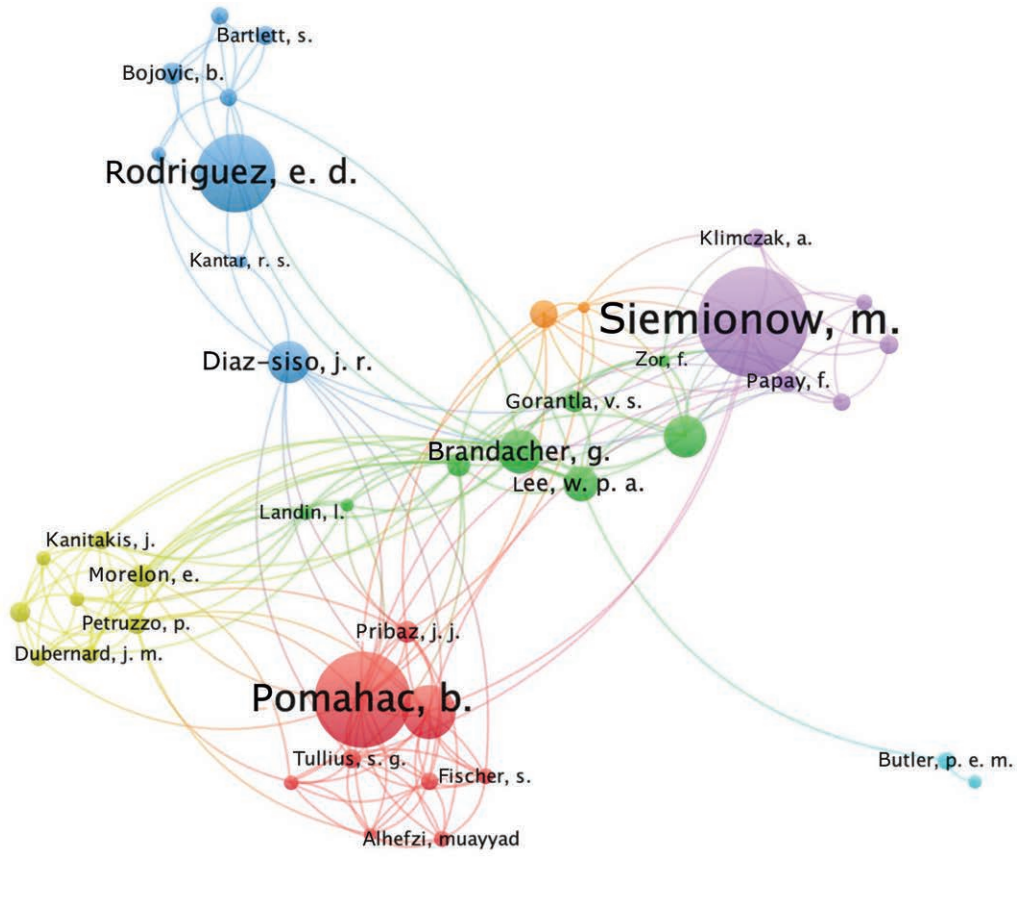


Fig. 2. VOSviewer co-authorship map.

Focusing on FT outcomes publications, 71% reported both long- and short-term outcomes (Fig. 6). Immunological outcomes were the most presented, followed by functional, aesthetic, and psychosocial outcomes (Fig. 7). The majority of these results were physician-reported, with a minority (28%) being patient-reported outcomes (PROs).

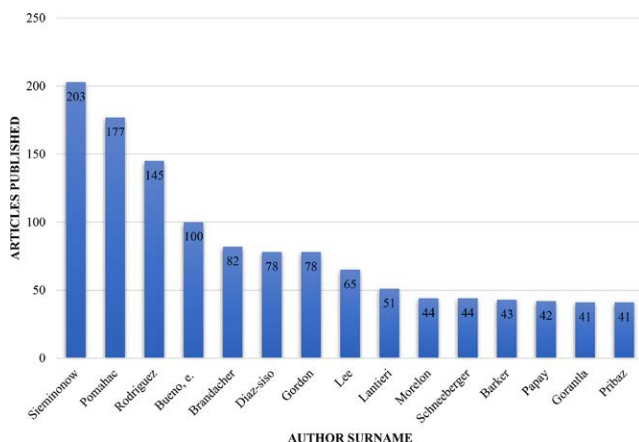


Fig. 3. The top 15 authors in the FT literature based on VOSviewer program analysis of publication frequency.

Trends over Time

The ethics, op-eds category demonstrates a steady trendline. The preclinical cadaveric model subcategory had a decreasing trend, whereas the preclinical animal model subcategory showed a steady increase over time. The clinical surgical techniques and clinical experiments and clinical outcomes subcategories both showed an increase over time, although the increase of clinical outcomes was at a slower rate. Excluding the year 2020, where there was a decrease in publication frequency in all subcategories, the facial transplant literature published over the past two decades is increasing (Fig. 8).

DISCUSSION

Evolution of the Facial Transplant Literature

The overall volume of the FT literature has rapidly expanded, in keeping with our hypothesis (Fig. 8). The first successful FT in 2005 marked the start of an upward trend in FT literature.

Many of the early FT publications, starting in the mid-1990s until the first successful FT in 2005, focused on the ethics and feasibility of these procedures. Before a successful FT, there were many considerations that required careful thought and discussion, including immunology,

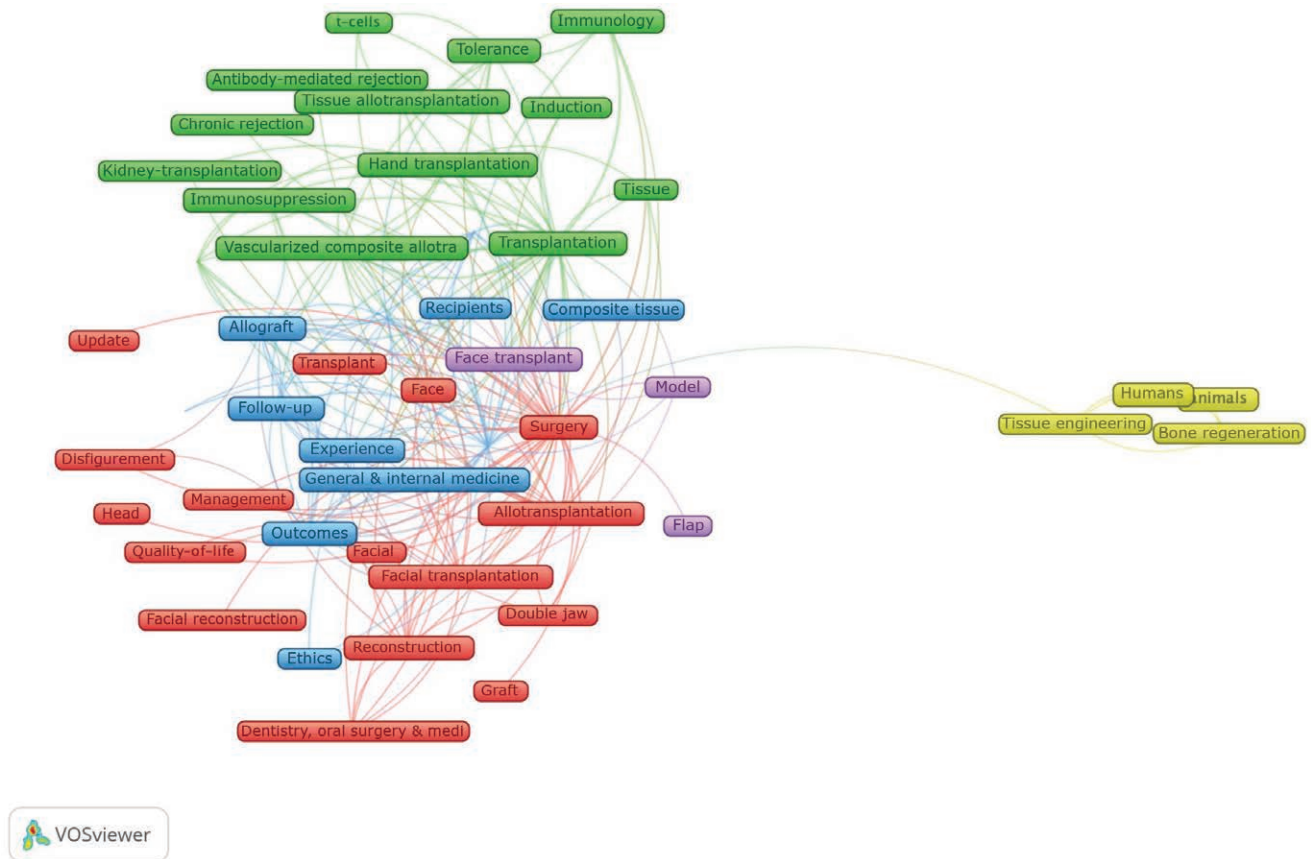


Fig. 4. VOSviewer keyword map to confirm and justify previously established categories in the FT literature.

pathophysiology, anatomy, psychosocial effects of FT, among other factors. The literature grappled with the ethical aspects of providing a patient with a new face, one accompanied by new facial features, leading many to wonder if patients would have the ability to recognize themselves in mirrors.¹⁵

Research also reported on psychosocial concerns of how society would perceive a patient in public due to atypical facial features posttransplant, and how a patient's own fears about onlookers' perceptions during social reintegration would impact the patient. Patients would likely need to cope with the psychosocial impact of their visible surgical scars and nonverbal cues from both strangers and loved-ones.¹⁶

Moreover, given the novelty of this procedure, patients would garner public recognition due to media coverage. This provides a tension to most recipients' primary urge to better fit in with society after the procedure; although many patients seek FT to gain social anonymity, the media coverage of FT recipients makes this close to impossible.¹⁷

Following the first successful FT, ethics-driven pieces decreased, likely due to increased societal acceptance following a clinical success. Interestingly, we observed a rise in ethics pieces in recent years, primarily focused on pediatric and cross-sex FT.^{18,19}

Early publications also included preclinical studies to investigate the feasibility and technical aspects of a

transplant. Cadaveric dissections allowed surgical teams to prepare for the unique challenges of performing an FT, and establish a surgical plan as well as back-up plans if obstacles arose during an attempt at FT. As expected, preclinical cadaveric studies displayed a similar decrease to ethical publications following the first FT, although it was delayed a few years. New centers preparing for their own FT in part explain the continued importance of cadaveric studies in the years immediately following the first FT. Centers also continued using cadaveric models to refine surgical techniques and subsequently published on the lessons and technical aspects they discovered.

Unlike preclinical cadaveric models, animal/translational models have remained relatively proportional over time, likely due to their utility for studying transplant immunology. Recent studies have investigated potential rejection biomarkers, important biological pathways, and long-term treatment efficacy of immunosuppressive regimens.^{20–23} Given the immense importance of transplant immunology and the push for safer immunosuppressive regimens, it could be expected for translational models to remain an important part of future publications.

As would be expected following the first FT, with the increase in FTs performed, there has been a significant increase in clinical publications. Centers worked

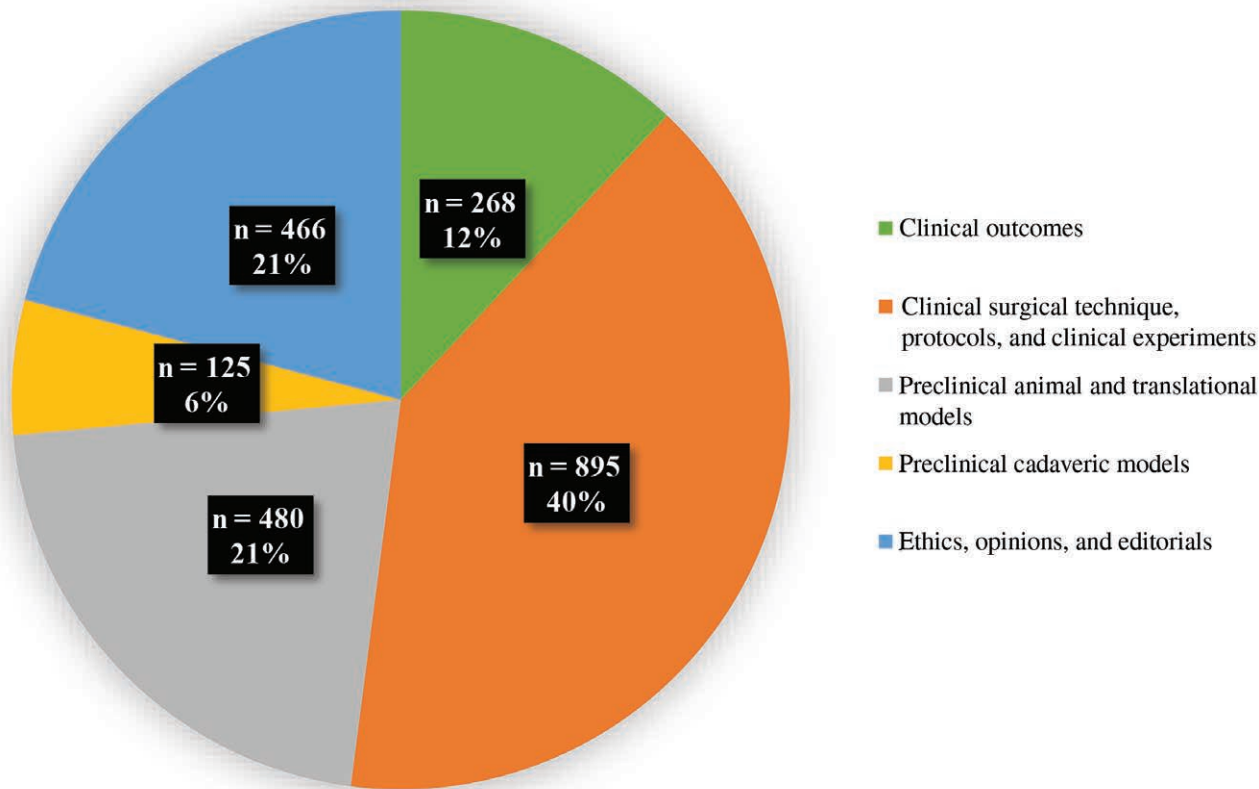


Fig. 5. Categorical breakdown of articles published on FT.

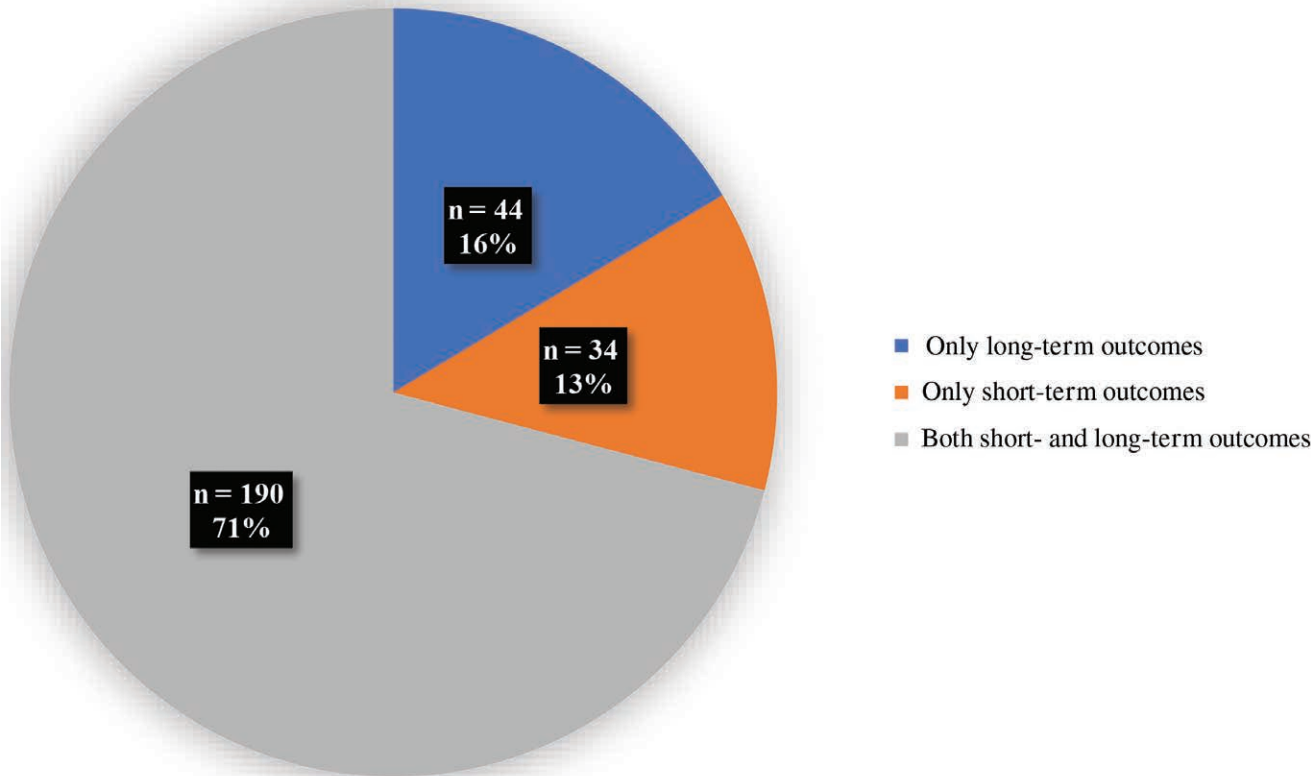


Fig. 6. Short-term vs long-term clinical outcome reporting.

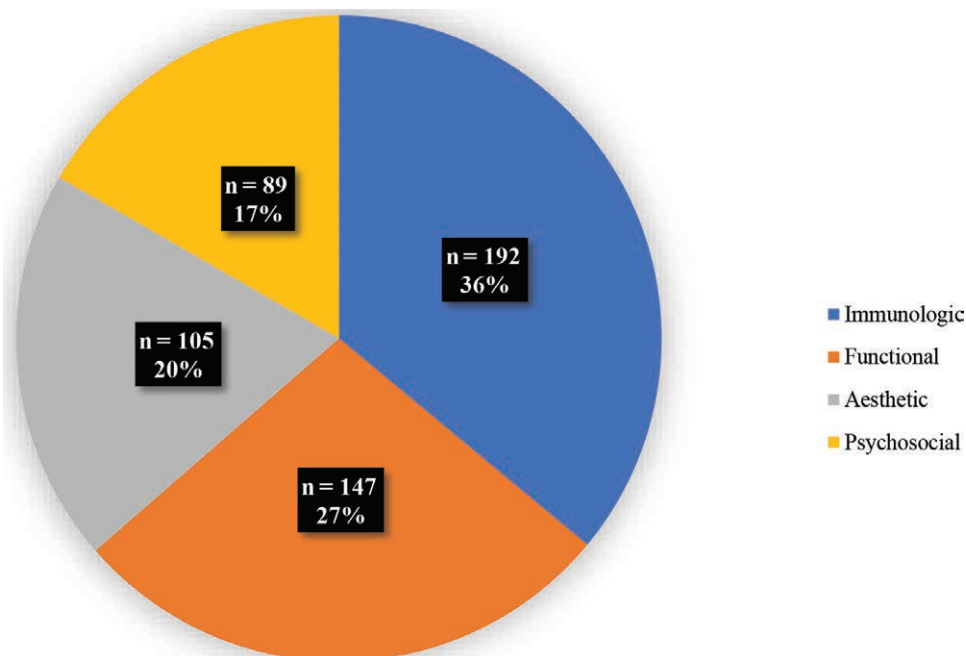


Fig. 7. Subtypes of clinical outcomes publications.

to present their operative experiences and immediate postoperative results. Immunological studies represent the largest outcome subcategory in the literature, likely because allograft rejection is one of the most significant concerns following FT.^{24,25} Despite rapid developments and improvements in our immunosuppression regimens, approximately 85% of patients will experience acute rejection despite systemic immunosuppression.²⁶ Remaining areas for investigation in FT immunology include less invasive screening modalities, long-term immunological outcomes, and clinical outcomes of less toxic regimens.

Gaps in the Literature

Significant knowledge and publication gaps exist on long-term outcomes greater than 5 years after FT, in addition to PROs and psychosocial outcomes. The field is now more than 15 years removed from the first FT, and little is known on the long-term survival and functionality, both of which were areas of ethical discussion before the first FT. As more FT recipients near a decade post-FT, detailed reports on the current level of function, QoL, and immunological outcomes are needed. These will be important to create a timeline for transplant viability and immunological status, which could inform discussion on the ethical concerns of pediatric FT.^{27,28} To ensure accurate comparison between FT centers, there should be standardization of outcome reporting methods.

The patient perspective is lacking in the literature. Many of the outcomes present in the literature are from the viewpoint of the transplant team, with only 28% representing PROs. The utility of PROs is well documented in both surgical and nonsurgical fields, with some

considering them essential. PROs can assess many important outcomes of FT. Patients presenting for FT evaluation have often suffered significant social stigmatization.¹⁵ As a result, the psychosocial effects of FT can be considered just as important as the functional ones. Psychosocial outcomes can evaluate the secondary outcomes of FT, including going out in public without hiding their face, eating in public, and improved verbal communication, among others.

Challenges with preoperative evaluation and donor identification, or successes with innovative ways to connect potential donors with FT teams, is not currently well-documented in the literature. Improving this aspect of the FT process can help ensure maximization of the already limited donor pool. Additionally, intraoperative and postoperative complications are not well documented but can highlight areas for improvement and serve as learning opportunities for future attempts. Detailed immunological reporting on rejection episodes, immune status, and efficacy of drug regimens can inform surgeons and patients alike, as well as facilitate research towards safer regimens. Although experience sharing and comparing outcomes will likely benefit the field at large, no current standard exists, limiting associations that can be made between data from different centers.

VOSviewer Collaboration Analysis

Each FT offers a learning opportunity not only for the transplant team, but for the field at large. Given the importance of crosstalk and collaboration between transplant centers, we assessed the interconnectedness of the literature. We identified five main clusters, as seen in Figure 2, with different colors identifying each cluster.

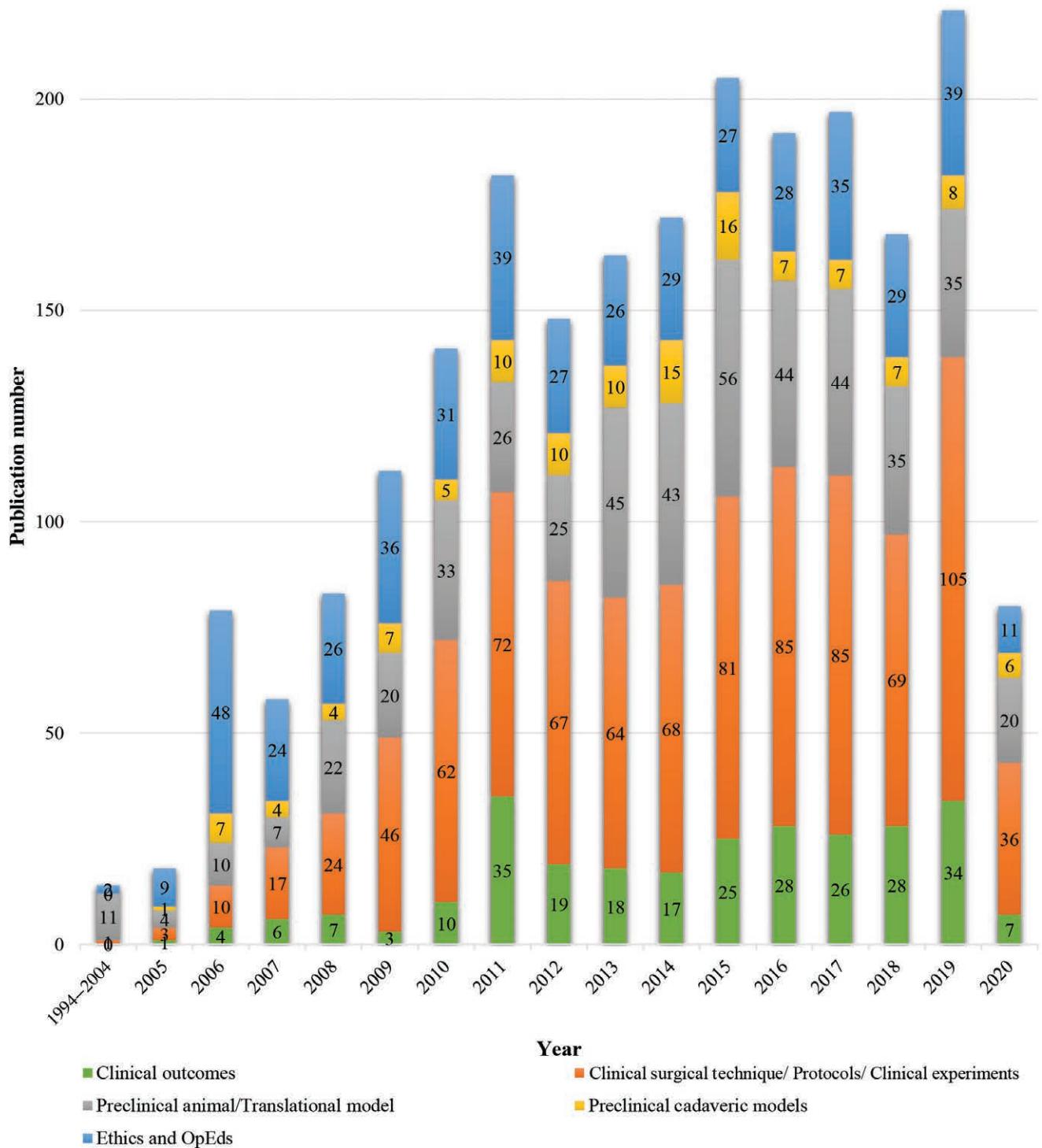


Fig. 8. Chronological trends in publications.

We found high levels of collaboration with 84.8% of the top 1000 authors in the field linked by a co-authorship network. Most of the main clusters had a primary author, denoted by the largest node, with connections to several other authors within their cluster and some connections between clusters. However, more of the connections were within clusters rather than between clusters, leading us

to believe the results of collaboration are likely an over-representation. Therefore, the collaboration data may be driven higher by greater communication between authors from the same institution, as opposed to authors from separate institutions.

From the five main clusters, all but one is in the United States, and all have performed at least one FT. Dr.

Sieminonow was involved in 2% of the FTs, but made up 9% of the literature, Dr. Pomahac, 19% of FTs and 8% of literature, and Dr. Rodriguez 6.5% of both FTs and publications (Table 2). These authors have each made substantial contributions to our current knowledge and experience with FT. However, when looking beyond the top five authors, who have contributed to 30% of the clinical FT experience, there are significantly fewer publications from those involved in the remaining 60% of FTs. A more significant contribution from these other centers would be a valuable addition to the field and facilitate the continued progress of FT.

It is important that all institutions are represented in the academic sphere, regardless of amount of funding, as this provides the most accurate representation of the field and facilitates maximal benefit to future patients. Institutional collaboration could address financial barriers in resource-limited areas.²⁹

Limitations

A limitation to our study was that data were collected for only half of the year 2020, due to data collection ending in July 2020. Additionally, changes such as quarantine, lockdowns, and a redeployment of effort to focus on caring for COVID-19 patients may have impacted FT publications. Our study is limited by the potential exclusion of relevant non-English papers, or any other relevant papers not identified by our search strategy. Last, given the methodology of bibliometric studies, we do not account for the quality of publications, and all publications are treated as equivalent. However, we feel our analysis provides a broad view of the field of FT with a focus on the areas of focus that remain unanswered.

CONCLUSIONS

Our analysis provides a detailed overview of the growing body of FT literature. Since 2005 when the first FT was successfully completed, there has been a rapid expansion of the FT literature and our knowledge of the topic. To ensure continued growth and development of the field, an increased focus on patient-reported, long-term outcomes and improvements in transplant immunology are needed. Moreover, transparent outcomes reporting should be encouraged. Our study results can help to inform future collaboration between authors and across face transplant programs to address gaps identified in the literature and ensure sustainable, well-documented development of the field as it continues to expand.

Table 2. Comparison between the Top 5 Authors' Quantity of FTs Performed and Publications through 2020

Top Authors	Percent (%) of Total FTs Performed	Percent (%) of Authorships in the FT Literature
Sieminonow	2.13	9.30
Pomahac	19.15	8.11
Rodriguez	6.38	6.65
Bueno	19.15	4.58
Brandacher	2.13	3.76

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