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REVIEW

CLINICAL ANATOMY WILEY

Thirty years of Thiel embalming—A systematic review on its utility in medical research

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Abstract

In 1992, Walter Thiel described and embalming method that rendered "lifelike" tissues. Over the last 30 years, the Thiel method has been introduced worldwide for medical training and scientific purposes. This review examines research which can be linked to the use of Thiel embalming. A systematic review was performed to identify articles published in the following categories: research content, disciplines involved, sources and quantities of tissues deployed, and changes in research scope related to changes in the chemical composition of Thiel embalming. Four-hundred twenty-four publications were included. A number of adaptations to the original Thiel protocol were found, aiming to provide suitable tissue-substitutes in the development of emerging medical technologies or procedures. Musculoskeletal surgery, anesthesia and intensive care were the most common disciplines that used Thiel embalmed tissues for research. Anatomy and biomechanics played a lesser role. An increase over time was observed in research outputs related to the Thiel method, while the number of specimens used per study decreased. The main centers using Thiel embalming were in Graz, Dundee, Sapporo, Bern, Zurich and Ghent, which jointly accounted for more than 54% of all research conducted using this method. Following three decades of use, the Thiel method has evolved into being a well-established embalming technique for research purposes. Its future is challenged by the demanding requirements on both technical facilities and personnel, limitations of certain chemicals for use as fixatives, costs, and questions as to how "lifelike" the embalmed-tissues are from an objective standpoint, all of which warrants future investigations.

KEYWORDS
education, embalming, fixative, simulation training, tissue fixation, training program, workshop

1 | INTRODUCTION

Postgraduate workshops and procedure-based training on human postmortem tissues have gained increasing interest world-wide to learn and practice surgical and interventional skills and/or develop new techniques. Similarly, a variety of medical disciplines aim to promote the research and use of postmortem tissues for training under the most realistic "lifelike" conditions possible. While fresh or fresh frozen tissues have become more utilized in a number of training facilities, there are certain limitations to the use of unembalmed tissues, including the short half-life of usage and increased risks of infection. Contemporary or chemical embalming techniques on human

tissues have been established for undergraduate and postgraduate medical training and research which aim for realistic haptic and visual tissue characteristics when handling the tissues. At the same time, with embalmed tissues, there is less emphasis on a time constraint regarding tissue degradation and autolysis.

Walter Thiel first described an embalming method in 1992, which, as he described, rendered such human post-mortem tissues to be "lifelike," based on a mixture of ammonium nitrate, boric acid and ethylene glycol (Thiel, 1992) (Table 1). The so-called "Thiel method" is highly complex, in regards to both the preparation of the chemical agents and in their application. Chemical components are mixed subsequently in multiple steps before being used as an intravascular injection fluid, a visceral injection fluid, a full-emersion solution in a container, and a moistening solution. Thiel himself stated in his first publication that his procedure was based on trials with as many as 977 corpses over a course of 30 years of development before he published his method. During this timeframe, human postmortem tissues were mainly used in undergraduate medical teaching; whereas postgraduate training and human tissue-based research played a marginal role.

When Thiel first published his method, the predominant feature he described was the "lifelike" color of the tissues (Hammer et al., 2015; Thiel, 1992). While the original composition of Thiel embalming especially accounts for the color realism of tissues, tissue pliability, and enhanced joint motion make this method, a popular choice nowadays as it is particularly suitable as a tissue-substitute for surgical intervention training. Furthermore, Thiel-embalmed tissues have less odor when compared to tissues embalmed by formaldehyde-based methods, which helps to increase the time of use of the tissues significantly.

Over the last 30 years, Thiel embalming has been introduced worldwide in Europe, North America, Asia, and Oceania predominantly in university-associated human anatomy and surgical training laboratories. Its primary use has been for medical training purposes, and as a consequence, Thiel-embalmed tissues have been a valuable, already-available resource for human tissue-based research. Thus, Thiel-embalmed tissues have emerged as an attractive alternative to fresh (frozen) tissues for medical training. It had been unforeseeable how Thiel embalming would be used three decades after its first description and how its original chemical composition would be modified to suit the needs in undergraduate and postgraduate medical education as well as in research. While the use of Thiel embalming for postgraduate training has been established broadly, the question remains as to whether Thiel-embalmed tissues have also become a mainstay and suitable tissue-substitute in applied research in human anatomy, in preserving tissue morphology and mechanical properties.

This systematic review aims to assess peer-reviewed research articles linked to the use of Thiel embalmed tissues. With 30 years elapsed since it was published, it is timely to assess which areas of applied research can be identified and what nature of research is best suited using Thiel embalmed tissues.

It is hypothesized that there is a clear trend toward increased research outputs as a function of publications over time and that more university-based anatomy and medical research centers are using Thiel embalming. Furthermore, it is hypothesized that the adaptations to the original chemical components of the Thiel method influenced the suitability of the tissues for use in training and research, with subsequent alterations in the publication outputs of different subject disciplines that make use of such embalmed-tissues for training and research.

2 | METHODS

A systematic review of the literature was performed to identify articles published from 1992 up until March 19, 2022, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). The search for articles occurred in the following online databases: PubMed, ScienceDirect, Scopus and Web of Science. The following keywords related to Thiel embalming were searched: "Thiel" AND ("embalming" OR "fixation" OR "cadaver").

Articles were included if they contained specific information on tissues embalmed according to the Thiel method or research related to Thiel embalming.

2.1 | Allocation of articles to predefined criteria

Following article retrieval, each manuscript was carefully examined before being categorized according to the following criteria:

Content was evaluated based on the following categories of technical (=focus on researching the feasibility of new techniques in the context of surgical or anatomical study), procedural (=focus on comparing different types of interventions when used by participants or interventionists), morphological (=studies on structural aspects of tissues with or without a link to a clinical discipline), biomechanical (=research on mechanical properties), reviews, and other (i.e., none of the aforementioned).

Types of tissues were categorized based on anatomical regions.

Disciplines were identified and categorized into the following fields of anesthesia and emergency medicine, anatomy, biomechanics, dentistry, ENT (otolaryngology), gynecology, imaging, surgery (cardiac, general/visceral, maxillofacial, musculoskeletal, neurosurgery, plastic, vascular) and urology.

Countries and *cities* were categorized on the basis of the identifiable source of the tissues, that is, location or site of the anatomy departments or tissue provider. Universities or research laboratories were only listed by the name of the city where the research was conducted except if there was more than one tissue provider of the embalmed tissues. In cases where no source of the tissues could be identified, corresponding authors were contacted for further clarification.

TABLE 1 Chemicals involved in the four most commonly used variants of Thiel embalming

	Injection/arterial infusion				Viscera/venous infusion				Container (ton) solution				Moistening/short term storage solution			
	Thiel, 1992	Thiel, 2002	Eisma et al., 2013	Hammer et al., 2015	Thiel, 1992	Thiel, 2002	Eisma et al., 2013	Hammer et al., 2015	Thiel, 1992	Thiel, 2002	Eisma et al., 2013	Hammer et al., 2015	Thiel, 1992	Thiel, 2002	Eisma et al., 2013	Hammer et al., 2015
Ammonium nitrate	+	+	+	+	+	+	+	not used	+	+	+	+		not given		
Boric acid	+	+	+	+	+	+	+		+	+	+	+	+		+	∅
Chlorocresol	+	+	+	+	+	+	+		+	+	+	+	+		+	+
Alcohol	∅	Ethanol	+	∅	Isopropanol	Ethanol	+		∅	Ethanol	∅	∅				
Formaldehyde	+	+	+	+	+	+	+		+	+	+	+				
Hot (tap) water	+	+	+	+	+	+	+		+	+	+	+	+		+	+
(Ethylene) glycol	+	(Propylene) glycol	(Propylene) glycol	+	+	(Propylene) glycol	(Propylene) glycol		+	(Propylene) glycol	(Propylene) glycol	+	+		(Propylene) glycol	+
Morpholine	∅	+	+	∅	+	+	+		∅	∅	∅	∅				
Potassium nitrate	+	+	+	+	+	+	+		+	+	+	+				
Sodium sulfite	+	+	+	+	+	+	+		+	+	+	+	+		+	∅
Total number of chemicals	8	10	10	8	10	10	10		8	9	8	8	5		5	3

Note: Chemicals subject to change were highlighted when compared to the original "1992 protocol" (Thiel, 1992). A trend toward applying significant quantities of alcohol as part of the protocol has been observed, likely with the objective to optimize tissue characteristics for musculoskeletal training and research purposes.

2.2 | Statistical analyses

The data analysis was conducted using Prism version 9.3.1 (GraphPad Software Inc., La Jolla, CA, USA) and Microsoft Excel version 16.49 (Microsoft Corp., Armonk, NY, USA). Normality was assessed using a D'Agostino and Pearson's test. Correlations were assessed based on the Spearman test.

3 | RESULTS

Following screening for eligibility according to the PRISMA scheme outlined in Figure 1, a total of 424 publications were included over the given time frame. Four-hundred were research studies further specified below, 18 review articles, and six articles that consisted of commentaries, editorials or replies. The research conducted using Thiel embalmed tissues could be attributed to a specific site of tissue provision in 398/400 studies (99.5%). In the remaining two studies (0.5%; one German, one Australian), the source of the tissues, that is, the location of the tissue providers or anatomy department, could not be determined.

3.1 | The original Thiel embalming method has been amended in multiple ways and ethanol being introduced to tailor tissues especially for postgraduate purposes

Based on the citations found in the research articles, the original composition described by Walter Thiel or its modification, that is, the "1992" (Thiel, 1992) or the "2002" protocol (Thiel, 2002) and its adaptations (Eisma et al., 2013), have been introduced in a majority of the research articles. A shift toward the "2002"-protocol (Thiel, 2002) to include significant quantities of ethanol was especially found at larger centers of providing post mortem tissues in research. Further adaptations to the existing protocols have

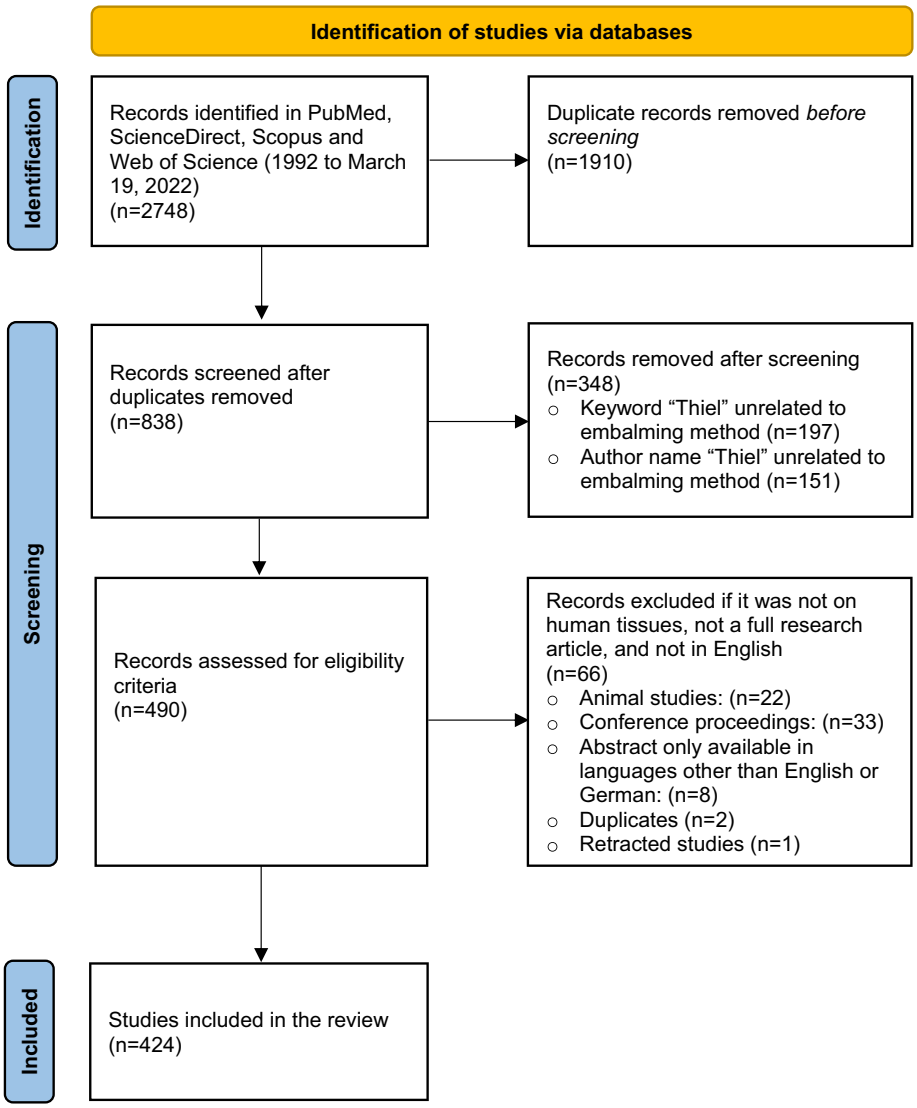

FIGURE 1 PRISMA flow chart (Page et al., 2021)

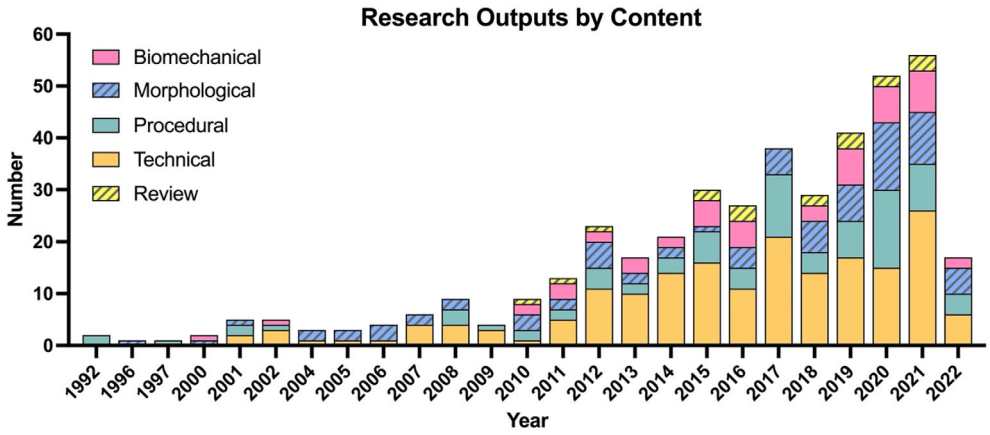

FIGURE 2 Research publication outputs by content related to Thiel embalming over the past 30-years. Combined technical or procedural research form a majority of studies published, whereas morphological or biomechanical studies contribute to the overall numbers to a lesser extent

been published, in an attempt to make the tissues more applicable for specific needs, for example, space or cost effective (Crosado et al., 2020; Hammer et al., 2015), or to adapt the chemical composition to enhance tissues suitability under more strenuous environmental conditions of non-climatized facilities in tropical areas (Reddy et al., 2017). Other adaptations have been introduced to enhance suitability of use in the training and development of emerging interventional techniques including radiofrequency ablation (Liao & Wang, 2019) and clinical imaging techniques (Gueorguieva et al., 2014). A recent focus has become the assessment of the antimicrobial capacity of Thiel embalming in comparison to other embalming compositions (Balta et al., 2019).

The number of chemical components involved in the embalming steps of the Thiel method remained comparably high in comparison to other commonly used embalming methods (Table 1). Thiel includes eight to ten components for the (arterial) injection solution, ten components for the viscera/venous solution (if applied), eight to nine components for the container solution, and three to five for the moistening or short-term storage solutions (Abarca-Olivas et al., 2014; Hammer et al., 2015; Thiel, 1992, 2002). The total number of chemicals used for all steps ranged from eight to ten chemicals for these protocols.

3.2 | Various tissues were studied using Thiel embalming

The total number of documented specimens used to answer the various research questions in a research article ranged from one to 702, with the total number of full-corpses documented ranging from 1 to 118. Institutions based in Graz (Austria) and Dundee (United Kingdom) published a majority of the studies with large specimen numbers. The types of tissues studied were most often derived from the pelvis and lower extremity ($n = 84$), followed by the head ($n = 58$), upper extremity ($n = 52$) and trunk ($n = 18$). A weak decline in specimen utilization has been observed over time, that is, the Spearman correlation yielded a decrease in the number of specimens used per study over time of ($r = -0.156$, $p = 0.023$).

3.3 | Research articles using Thiel embalmed tissues have a narrower scope

Overall, Thiel embalmed tissues served as the primary objective to address technical ($n = 186$) and procedural ($n = 84$) research questions or descriptions involving post mortem tissues. Morphological ($n = 79$) and biomechanical ($n = 51$) research questions were less prevalent, accounting for 18.6% and 12.0% of the included articles, respectively (Figure 2). Details on the retrieved research can be found in Data S1 and a full list of references in Data S2.

3.4 | Medical disciplines that used Thiel-embalmed tissues

The predominant medical disciplines that used Thiel embalmed tissues for research questions were surgical disciplines ($n = 263$) and anesthesia & intensive care ($n = 72$; Data S1 and Data S2). Within surgical disciplines, musculoskeletal ($n = 141$), general & visceral ($n = 32$), ENT ($n = 25$), vascular surgery ($n = 12$) used Thiel embalmed tissues to address their scientific objectives. Urology ($n = 15$), neurosurgery ($n = 11$), plastic surgery ($n = 8$), gynecology ($n = 4$), maxillofacial ($n = 13$) and cardiac ($n = 2$) surgery made sparse use of Thiel embalmed tissues for their research thus far.

Dentistry ($n = 7$) was also only occasionally the discipline of focus in these studies. Figure 3 graphically summarizes the five most commonly observed disciplines amongst the included research articles.

The shift toward the "2002" protocol (Thiel, 2002) was associated with a gradual change and increase in different subject disciplines using Thiel embalmed tissues for research. This change toward the use of the Thiel method seemed to be advantageous especially for musculoskeletal-related research as well as for research in anesthesia and emergency medicine, as reflected by both the absolute and relative increase in the numbers of publications (Figure 3).

In 47 studies, anatomy, which mainly included morphological studies, could be attributed as the primary specialty discipline, with certain research focus toward procedural ($n = 18$) and technical ($n = 7$) aspects. Only 10% of all studies conducted with Thiel

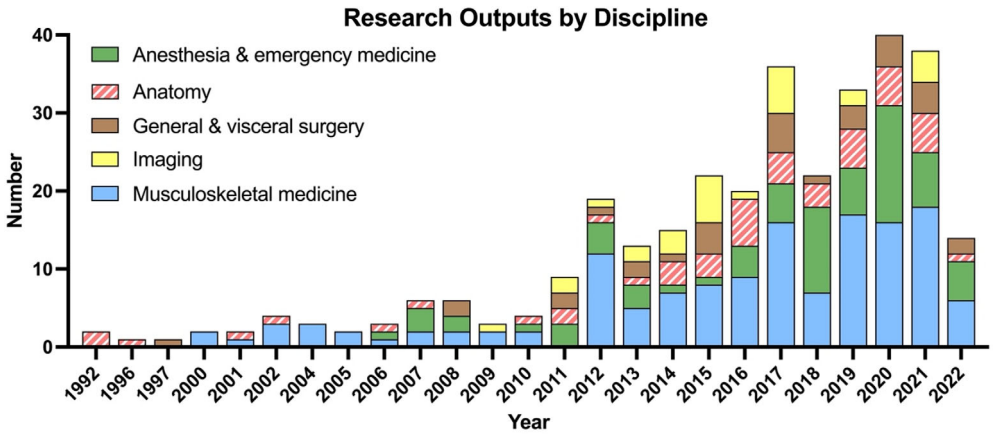

FIGURE 3 Research publication output by discipline related to Thiel embalming over the past 30-year course. Thiel tissues if used for research were most commonly studied in the context of musculoskeletal medicine or anesthesia and emergency medicine

embalmed tissues have been in the focus of anatomy research over the last 5 years. Imaging was found to be the primary research discipline in 28 studies in total.

There has been a moderate to strong increase in published research related to Thiel embalmed tissues in certain disciplines over the course of time. The correlation of increased number of research publications was strong amongst musculoskeletal-related research ($r = 0.83$) and anesthesia and emergency medicine ($r = 0.89$), followed by general & visceral surgery ($r = 0.73$), ENT ($r = 0.74$) and anatomy ($r = 0.67$; all $p < 0.001$), with a moderate correlation observed in imaging ($r = 0.56$; $p = 0.004$) and urology ($r = 0.46$; $p = 0.02$).

3.5 | The core users of Thiel embalming for research are based at six centers

For the ease of reference, the following results have been organized according to global regions and geographical locations. Figure 4 summarizes the output of research articles by country, and Figure 5 by city. More detail on the individual publications can be found in Data S1 and Data S2.

Europe: Thiel embalming has predominantly been used for research purposes on human postmortem tissues at European institutions. Beyond Graz (Austria; $n = 92$ studies), three other Austrian centers account for less than two studies each at center (Innsbruck, Krems an der Donau, Salzburg). In Germany, three centers generated a larger output of publications (Bochum $n = 6$, Münster $n = 9$, Ulm $n = 6$) and six centers with smaller outputs ($n = 19$; Aachen, Heidelberg, Kiel, Leipzig Mainz, Munich, Tübingen) could be identified. Belgium has one larger center (Ghent $n = 15$) and Spain two larger centers (Alicante $n = 8$, Madrid $n = 11$) as well as four smaller centers ($n = 4$; Barcelona, Elche, Malaga, Salamanca). Research involving the Thiel method has further been published from centers in France ($n = 6$; Caen, Dijon, La Tronche), Hungary (Budapest $n = 2$), Italy (Padova $n = 2$), Czech Republic (Prague $n = 1$), Ireland (Cork $n = 9$), Malta (Msida $n = 3$), Poland (Kraków $n = 1$), Portugal (Porto $n = 1$), Slovenia (Maribor $n = 3$) and The Netherlands (Groningen $n = 5$). Three Swiss centers showed high research activity using Thiel embalmed tissues (Basel $n = 7$, Bern $n = 28$, Zurich $n = 19$); and two Swiss centers occasionally used Thiel embalmed tissues for research ($n = 4$, Fribourg, Geneva). The United Kingdom has grown to be the country with the second highest number of publications using Thiel embalming, especially at Dundee ($n = 60$) and three other smaller centers ($n = 7$; Cardiff, Leeds, Nottingham).

Asia and Oceania: Thiel embalmed tissues have only been used at a smaller scale for output of research publications in Asia, namely in India ($n = 4$; Kerala, New Delhi, Rishikesh), Philippines (Manila $n = 2$), South Korea (Seoul $n = 1$), Thailand (Bankok $n = 1$) and Turkey (Kocaeli $n = 1$). In Japan, Sapporo ($n = 19$) and Tokyo ($n = 9$) have utilized Thiel to a much greater extent, followed by a number of other smaller centers that spread over the country ($n = 20$; Aichi, Ehime, Hiroshima, Kagawa, Kanazawa, Kitakobayashi, Masumaya, Mibu, Nagasaki, Nagoya, Niigata, Okayama, Tohoku, Yokohama, and Yonago). Thiel embalming was brought to New Zealand in 2015 (Dunedin $n = 6$) which remains the only country in Oceania where this method has been used frequently in postgraduate teaching and research.

Americas: In Canada, Montréal ($n = 10$) and Trois-Rivières ($n = 5$) have published articles based on Thiel embalmed tissues, followed by two centers with a smaller output of publications ($n = 3$, Laval, Toronto). In contrast to the higher demand for teaching resources in the United States of America, Thiel has only been used sporadically ($n = 5$; Ann Arbor, Commonwealth, Kirkville, Springfield IL) based on the included articles. The only center in South America identified was in Chile (La Frontera $n = 1$).

Further analysis shows that as few as six centers account for 54.5% of the total research publication outputs based on tissues embalmed with the Thiel method (Figure 4). This proportion has remained steadily high amongst these centers for more than a decade. Graz and Dundee were the main contributors, jointly accounting for 35.8% (152 studies) of all research with Thiel embalmed tissues over the 30-year time frame; Austria and United Kingdom together accounted for 39.4%. While output of research articles from Graz can be dated back to the early days of its publication of the Thiel method in 1992, Dundee, Zurich, Bern, Munich and Sapporo have only first began using Thiel in the time frame between 2007 and 2013.

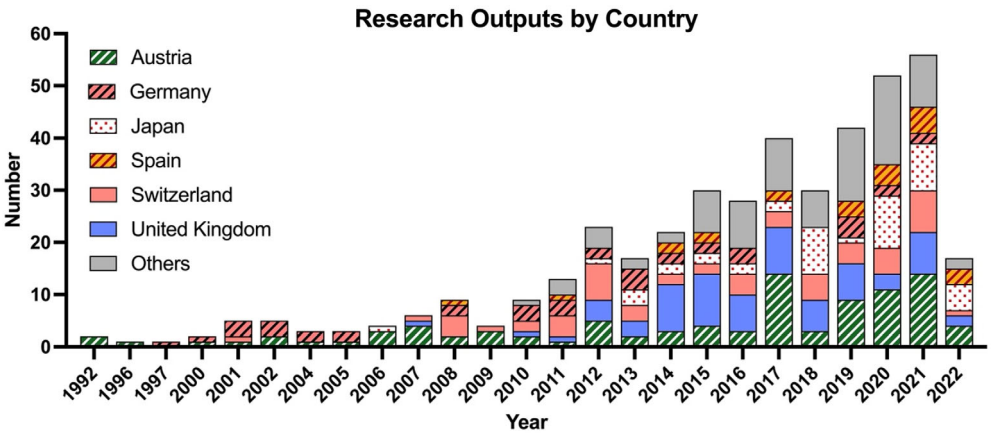

FIGURE 4 Research publication output by country related to Thiel embalming over the past 30-year course. European countries including Austria, Switzerland and the United Kingdom can be considered the countries with the largest of such research outputs

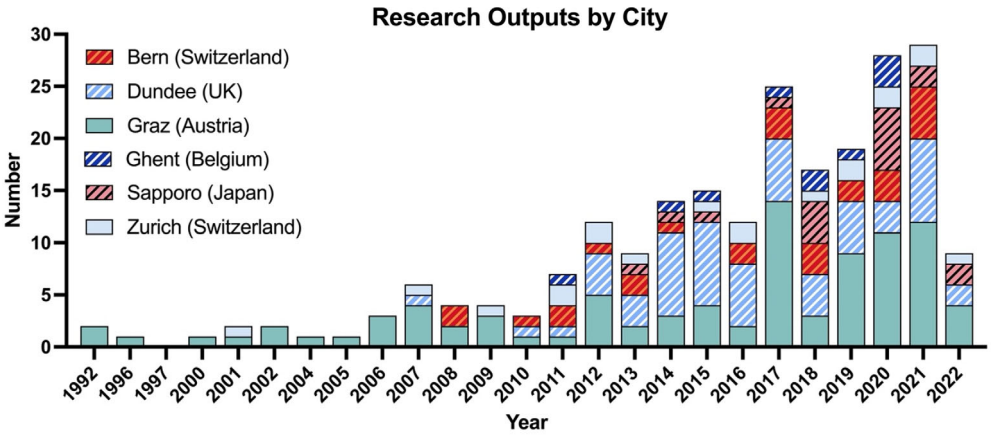

FIGURE 5 Research publication output by City related to Thiel embalming over the past 30-year course. Graz, Dundee, Bern, and Sapporo can be considered the most active sites where Thiel embalmed tissues are used for research

4 | DISCUSSION

Over the last three decades, the Thiel method has become an established technique for embalming human postmortem tissues. It complements other embalming techniques, providing "lifelike" tissue features (Bilge & Celik, 2017; Hayashi et al., 2014; Wedel et al., 2019) in comparison to the use of fresh (frozen) tissues. Research articles related to investigations of post mortem tissues embalmed with the Thiel technique have increased over time following the first introduction of the method in 1992. The Thiel method has been a mainstay embalming technique at a number of anatomy centers predominantly in Europe as well as Japan. For the remaining parts of the world, the use Thiel-embalmed tissues for research purposes has been sparsely identified based on the included publications in this review. Owing to the complexity of chemical components and steps involved in the Thiel method, the number of centers that employ Thiel embalming remained relatively low in spite of some of the advantages this method provides, including the perception of a "lifelike" appearance of tissues and increased tissue pliability especially in muscle tissues and joint regions.

In consequence, increasing research outputs could be found, however, conducted in a relatively low number of research centers, providing evidence against the first hypothesis. There is a broad diversity of research conducted in various research fields deploying traditional, established and novel techniques in combination with embalmed post mortem tissues. This research helps support the advancement in medicine, especially in surgery, anesthesia and intensive care. Anatomy has the privilege to form one of the cores of this translational research, and Thiel embalmed human tissues have certainly facilitated this process.

Owing the diversity of disciplines, techniques and method adjustments achieved over the years with the Thiel embalming, this systematic review has intentionally limited in-depth discussion of specific research details in favor of providing a meta perspective of general research directions and centers involved.

4.1 | The use of Thiel embalmed tissues in undergraduate and postgraduate medical training and output of research publications appear to be closely linked

There appears to be a complex interplay of tissue availability for under- or post-graduate medical teaching and for research related to these tissues (personal communication amongst the six major centers described above). It appears that with more tissues available for undergraduate training, the more tissues are also be available for research and thus greater publication outputs. This logic applies

especially to larger centers using the Thiel technique, where there is reciprocal feedback generated between tissue providers, (expert) training and research publications. Likewise, the experience gained by these institutions appeared to catalyze further refinements in chemical composition for both teaching and research. This scenario has been the case for Graz as well as for Dundee—both institutions had previously used Thiel embalmed tissues also for their undergraduate training (Eisma et al., 2013) and both institutions have generated considerable research publication outputs.

4.2 | Thiel embalming remains a sophisticated embalming method to apply

Compared to other methods of embalming, the Thiel method remains a complex technique, involving large quantities of various chemicals, and a number of demanding steps that require a highly skilled team and suitable facilities (Eisma et al., 2013; Hammer et al., 2015; Thiel, 1992, 2002). As many as eight to ten different chemicals are involved in the embalming procedure, two to three different combinations are used for fixation, with further combinations of agents involved with total submersion and moistening (Eisma et al., 2013; Hammer et al., 2015; Thiel, 1992, 2002) of tissues. Certain modifications have been proposed over the years (Eisma et al., 2013; Gueorguieva et al., 2014; Hammer et al., 2015; Liao & Wang, 2019; Reddy et al., 2017), however, with limited effect on user friendliness and ease of applicability.

An explosion-proof environment should likewise be considered in case if ethanol is involved (Hammer et al., 2015; Thiel, 2002). Further to this requirement, the chemicals in Thiel solutions are classified as corrosives, flammables, oxidizing agents, toxins, and substances harmful to the environment and especially to humans (Hammer et al., 2015). As a result of its toxicity profile and harmful properties of the chemicals involved, special protective measures must be taken into account to avoid such exposure when preparing and using Thiel embalmed tissues. Likewise, disposal of the chemicals involved in Thiel embalming is also challenging. For example, boric acid must not be disposed via public sewages to avoid introduction of such effluents into the aquatic environment. Boron compounds have been shown to be harmful for certain fish, crustaceans and algae (Harper et al., 2012; Schoderboeck et al., 2011). In fact, in Dunedin, New Zealand, waste containers of Thiel embalming solutions have been treated as hazardous waste and therefore are not disposed into the environment of the Pacific Ocean (own unpublished findings). At centers residing in more centralized continental areas, other methods of waste management exist that include fluid disposal into the public sewerage system only after a completing a degreasing step and pH level adjustment of the embalming solutions to be disposed.

4.3 | Past and present directions of research utilizing Thiel embalmed tissues

Regarding the areas of research conducted, a dominance of technical and procedural studies was observed (Figure 2). In this regard, Thiel embalming seems to have key advantages to other methods, with the perception of providing "lifelike" haptic feedback and optical appearance to tissues. Therefore, studies on new and emerging interventional techniques (technical papers) or on the comparison of different types of medical interventions (procedural papers) were found, at 43.9% and 19.8% of the included articles, respectively. These studies largely outweighed research on tissue morphological or biomechanical properties. The reasoning behind this trend away from morphometry is multi-faceted, and may be related to conflicting evidence on whether Thiel embalmed tissues provide "lifelike" tissue characteristics from an objective perspective, as will be outlined further below. In contrast to the initial "lifelike" impression on a macro scale, microstructural examination of Thiel embalmed tissues has revealed extensive tissue damage, especially in lipid-rich tissues such as nerves and certain connective tissues (Crosado et al., 2020).

Certain observations can be made over time involving medical disciplines using the Thiel embalming method in research. A trend of increased publication output in disciplines of musculoskeletal surgery, anesthesia and emergency medicine was seen (Figure 3), accounting for more than half of all published research output involving this method. This trend seems to be correlated with the introduction of the "2002" protocol (Thiel, 2002) and its modifications (Eisma et al., 2013) as opposed to the original "1992" protocol (Thiel, 1992). The embalmed tissues using the "2002" protocol (Thiel, 2002) provides certain beneficial attributes, especially in musculoskeletal surgery, anesthesia and emergency medicine. The degreasing of the tissues related to the application of ethanol in the "2002" protocol (Thiel, 2002) renders tissues more pliable and thus more suitable as tissue-substitutes. However, other tissues, especially in the viscera, become altered and are less suitable for use in research by the "2002" protocol (Thiel, 2002). For example, a brownish discoloration occurs in neck, thorax and abdominal tissues soon after contact with air. Further, ethanol-related shrinkage with deformation is observed. These combined effects shorten the half-life of use in for both training and research, especially if morphometries are involved. Such observations may help to explain the scarcer use of Thiel embalmed tissues in general & visceral surgery, ENT as well as urology. Therefore, the hypothesis that changes in the chemical composition of embalming made over the years influenced the nature and disciplines generating research outputs based on Thiel embalming can be confirmed.

4.4 | A challenging future

The use of Thiel embalming in an anatomy department is faced by four main factors: (1) the demanding technical requirements of the facility environment and expertise of the team, (2) limitations to the use of formaldehyde and other hazardous chemicals, (3) the increasing cost related to the chemicals, and (4) lacking data on the validity of the morphometries and tissue properties to date.

1. The demanding technical requirements of the facility environment and expertise of the team mainly impacts the ability of highly-

skilled staff to produce esthetic and lasting tissues with the desired properties. Further in this regard, the footprint of the large containers needed for total tissue submersion present a significant design-challenge, especially in new purpose-built facilities with limited space availability. For an effective use of space, the dimensions of containers have to be optimized to provide an optimal cost-use ratio. The duration of the submersion step in the Thiel method ranges between 6 and 10 months depending on the specific protocol being used. Especially for the "1992" protocol (Thiel, 1992), tissues are required to be submerged regularly between periods of use, in order to provide lasting and esthetic tissues. This combination of regular re-submersion results in significant logistical demands and low tissue throughput when compared to other embalming techniques such as formaldehyde or ethanol-glycerin (Hammer et al., 2015). In spite of these measures, the half-life of use is limited, as muscles, nerves and viscera become mechanically less resilient and change in color quickly.

2. Formaldehyde, which has gained increasing interest in tissue-embalming over recent years, has become classified a Type 1b carcinogen (National Toxicology Program, 2010), which now limits its use in embalming. The quantities of formaldehyde used for Thiel embalming are relatively low as compared to other embalming techniques (Thiel, 1992), and threshold exposure levels can be adhered to by simple incorporation of air extraction and exchange technology. However, the risk profile remains similar to other embalming techniques, especially for prosectors. Also, other substances of Thiel embalming have hazard profiles (Hammer et al., 2015). Certain precautions are therefore necessary to minimize any risks related to their exposure (Hammer et al., 2012).
3. The increasing costs of chemical supplies make Thiel embalming disproportionately more expensive than other methods. Some chemicals may be difficult to import into remote areas, or it may be more cost effective to use pre-mixed solutions. Another cost saving measure may involve the use of technical grade chemicals or recycling the container fluids. Nevertheless, the financial expenses in Thiel embalming chemicals are eight- to tenfold greater compared to ethanol-based techniques such as ethanol-glycerin (Hammer et al., 2012; Hammer et al., 2015) or Crosado (Crosado et al., 2020) embalming.
4. A number of tissue alterations have been reported in Thiel embalmed tissues (Crosado et al., 2020). These alterations include extensive acellularization with full disintegration of cell boundaries on a microscopic level, as well as dehydration, degreasing, discoloration, loss of intrinsic form and collapsing of tissue integrity on a macroscopic level. As a result, it cannot be assumed that morphometries are preserved (Grechenig et al., 2021), and morphometric studies using Thiel embalmed tissues may require validation against other (embalmed) tissues where the alterations are known to be minimal or closely akin to the fresh (frozen) state. Mechanical properties are altered to various extent in a time- and tissue-dependent manner which is matter of ongoing research (Fessel et al., 2011; Hammer et al., 2016; Hohmann et al., 2019; Liao et al., 2015; Verstraete et al., 2015; Wilke et al., 2011; Zwirner et al., 2019). While these observations seem less surprising with any embalming, these factors raise some questions on the "lifelike" features attributed to Thiel embalmed tissues.

This complex interplay of factors impedes establishing Thiel as a mainstay embalming method in recent days, which may partly be a rationale as to why the number of institutions that use the method for research seemed to have stalled. Along with its complexity in steps and less desirable features generated in the tissues for certain (post-graduate) settings, the Thiel method has been discontinued in certain departments following initial evaluation or use, which include Kiel, Germany and Dunedin, New Zealand (personal communications).

4.5 | On the future potential of Thiel embalming

Since the method of Thiel embalming was first introduced in 1992, it had undergone a number of alterations, namely the "2002" protocol (Thiel, 2002) and adaptations such as the changes by Eisma and coworkers (Eisma et al., 2013). These modifications correlate to an increase in the number of research publication outputs related to Thiel embalmed tissues which has been subject to this review. In spite of increased research publication output, Thiel method remains a sparsely used embalming technique limited to highly equipped anatomy facilities. Furthermore, its high financial costs, the lack of staff experienced working with this method, or equally suitable routes toward providing "lifelike" post mortem tissues challenge its utility. Nevertheless, once successfully established, the Thiel method has mostly continuously been used for various research purposes a number of institutions worldwide. Thus, it can be concluded that the advantages the Thiel method provides outweigh most of the aforementioned challenges in medical training. Overcoming these challenges on its impact on tissues at both a microscopic and macroscopic scale would further enable and expand research in various fields of anatomy, biomechanics and clinical medicine.

4.6 | Limitations

A number of limitations apply to this review. First, data retrieval was conducted in a given number of scientific databases and further restricted to research (abstracts) published in English or German. While anecdotal reports exist on the Thiel method being used in other territories worldwide, substantiating evidence could not be included if published in other languages. Further, research deploying Thiel embalmed tissues without specific mention of the technique could not be included in the search string. The allocation of the research to the given categories was based on the information made available in the respective papers, and was therefore leaves scope for interpretation. The same applied to the centers providing the tissues, though inter-institutional collaborations were considered especially in the German speaking countries.

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