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The current status of brachytherapy in Europe – A GEC-ESTRO Brachy-HERO survey

J.G. Johansen [a,b,*], I.M. Jürgenliemk-Schulz [c], H. Haddad [d], J.M. Hannoun-Levi [e], T.P. Hellebust [f], B. Guix [g], K. Loessl [h], B. Pieters [i,j], C. Rao [k,l], V. Strnad [m], A.E. Sturdza [n], L. Tagliaferri [o], Z. Takacsi-Nagy [p], E. Villafranca [q], P. Wojcieszek [r], A. Rembielak [s,t], P. Niehoff [u]

[a] *Aarhus University, Department of Clinical Medicine, Aarhus, Denmark*
[b] *Aarhus University Hospital, Danish Centre for Particle Therapy, Aarhus, Denmark*
[c] *UMCU, Radiation Oncology, Utrecht, the Netherlands*
[d] *Tuebingen University Hospital and Medical Faculty, Eberhard Karls University of Tübingen, Department of Radiation Oncology, Tübingen, Germany*
[e] *Antoine Lacassagne Cancer Center, Radiation Oncology, University Coete d'Azur, Nice, France*
[f] *Oslo University Hospital, Department of Medical Physics, Oslo, Norway*
[g] *Fundación IMOR, ATRYS, Radiation Oncology, Barcelona, Spain*
[h] *Inselspital, Bern University Hospital, University of Bern, Clinic of Radiation Oncology, Bern, Switzerland*
[i] *Amsterdam University Medical Center, University of Amsterdam, the Netherlands*
[j] *Cancer Center Amsterdam, Cancer Treatment and Quality of Life, Amsterdam, the Netherlands*
[k] *Imperial College London, Surgery and Cancer, London, United Kingdom*
[l] *Cumberland Infirmary, Colorectal Surgery, Carlisle, United Kingdom*
[m] *University Hospital Erlangen, Department of Radiation Oncology, Erlangen, Germany*
[n] *Medical University of Vienna, Radiation Oncology, Vienna, Austria*
[o] *Fondazione Policlinico Universitario Agostino Gemelli, IRCCS, Radiotherapy, Rome, Italy*
[p] *National Institute of Oncology, Department of Radiotherapy and National Tumor Biology Laboratory and Semmelweis University, Department Of Oncology, Budapest, Hungary*
[q] *Hospital Universitario de Navarra, Radiation Oncology, Pamplona, Spain*
[r] *MSC National Research Institute of Oncology, Gliwice Branch, Brachytherapy Department, Gliwice, Poland*
[s] *The Christie NHS Foundation Trust, Clinical Oncology, Manchester, United Kingdom*
[t] *The University of Manchester, Division of Cancer Sciences, School of Medical Sciences, Faculty of Biology, Medicine and Health, Manchester, United Kingdom*
[u] *Sana Kliniken Offenbach, Dep. Of Radiotherapy, Offenbach, Germany*

A B S T R A C T

A survey regarding utilisation of brachytherapy was distributed to European brachytherapy professionals. Eighty replies from 26 countries were received, two of which were outside Europe. The replies showed that brachytherapy is still widely used. The main indications for brachytherapy are gynaecological and prostate cancer, with >80 % of the responding countries performing brachytherapy for these indications. There is on average one brachytherapy centre per 0.8 million inhabitants, ranging from 0.4 per million to 2.3 per million inhabitants. The organisation of brachytherapy on national levels also varies from country to country, with less than half of the countries having a central brachytherapy registry. All in all, the survey shows that brachytherapy still plays a role on modern radiotherapy, but the field could benefit from a stronger collaboration both nationally and internationally.

1. Introduction

Brachytherapy (BT) has been an integral part of cancer treatment for more than a century. Its conformal dose distribution makes BT ideal for high-dose delivery to targeted areas. Clinical studies have shown that BT, either as monotherapy, a boost or for re-irradiation purpose, can improve the clinical outcome of gynaecological [1–3], prostate [4,5] and breast [6] cancers. Today, a BT boost is considered as the standard care for radiotherapy of cervical cancer [7], and in 2022, GEC-ESTRO published a recommendation to include a BT boost for prostate cancer [8]. From a health economic perspective, BT is an economical treatment modality compared to other radiotherapy modalities in terms of equipment investments. At the same time, it is an interventional procedure, which often involves several manual procedures and specialised

* Corresponding author at: Department of Clinical Medicine, Aarhus University, Palle Juul-Jensens Blvd 99, 8200 Aarhus N, Denmark.
E-mail address: jacjoa@rm.dk (J.G. Johansen).

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trained personnel. The utilisation might therefore be more impacted by available and adequately trained personnel compared to external beam therapy modalities, where an investment in e.g. modern linear accelerators or proton facilities leads to a long-term financial commitment from the hospital.

A central register, such as the list of particle therapy facilities provided by the Particle Therapy Co-operative Group (PTCOG) [9], does not exists for BT. Therefore, there is no reliable information available on the current use of BT in terms of indications treated, number of BT clinics and number of treatments performed per year in each country. The most recent pattern of care study was published in 2010 [10], where no clear change in patients treated with BT was observed between 2002 and 2007. However, more recent reports have shown a decrease in BT for cervical and prostate cancer in the US over the last decade [2,3,11], and an interview with BT experts across Europe indicated an overall declining trend for BT [12]. In 2023, the GEC-ESTRO Brachy-HERO working group initiated a serious effort to establish an overview of the current utilization of BT in Europe, similar to what has previously been done for external radiotherapy by the ESTRO-HERO group [13]. As a first step, a short survey was distributed to BT experts primarily in Europe through the national societies, with the aim of providing pilot data for more in-depth studies. A key motivation in performing the survey, beside gaining an overview of the clinical utilisation of BT in Europe, was to obtain an overview of possible registries and relevant

Table 1
A list of the questions and follow up questions given in the survey together with the possible answers. The questions are sorted after the categories in which they are presented in the article. Questions in italic has not been included in the current analysis.

Category	Question	Options	Sub-question	Options
	Have you already participated in our survey in 2022 sent to the national societies in 6/22	*Yes/No*		
Demographic overview	Please name the country where you work!	Free form		
	Have you been appointed by your professional society as the person responsible for brachytherapy in your country?	Yes/No		
	Is there a central register in which departments brachytherapy is offered?	Yes/No		
	Do you know at how many locations brachytherapy is offered in your country?	Yes/No	*If yes:* *How many are there* *If No:* *Is there any way to determine this number?*	*Total number/Number of Hospitals/* *Number of only outpatient facilities* *Yes/No*
Current brachytherapy utilization	In your country you use? [multiple answers allowed]	HDR Afterloader PDR Afterloader LDR implants Others		
	Name the most important indications for brachytherapy in your country. [multiple answers allowed]	Prostate Gynae GI (Upper GI and lower GI) Head & Neck Breast Sarcoma Paediatric tumors Eye Skin tumors Keloids Lung (Bronchus and interstitial) Liver Salvage for recurrence Other …		
Future utilization of brachytherapy	What do you foresee to be the most frequent indications in the future? [multiple answers allowed]	Prostate Gynae GI (Upper GI and lower GI) Head & Neck Breast Sarcoma Paediatric tumors Eye Skin tumors Keloids Lung (Bronchus and interstitial) Liver Salvage for recurrence Other …		
Clinical studies and trials	Are brachytherapy studies going on in your country?	Yes/No	If yes: What type of studies? [multiple answers allowed]	Phase III Trial Phase II Trial Monocentric study Clinical investigation Prospective register studies Others
	Other thoughts			

persons, which can be reached out to in future studies. This paper provides the initial findings from this survey.

2. Method

2.1. The survey

A survey consisting of ten questions (Table 1) was distributed to 35 national radiotherapy societies from the ESTRO database in May 2023. The national societies were asked to forward the survey to the responsible professionals for BT in their country. The questions were divided into four categories: demographic overview, current and future utilisation and clinical studies.

The survey was closed after two months in July 2023 after receiving 98 replies from 26 countries. Eighteen responses were excluded from the analysis. The only criteria for exclusion was an insufficiently completed questionnaire (<5 question answered). All 18 excluded responses came from countries, where at least one other response was analysed. Hence, a total of 80 responses were included in the analysis.

2.3. Analysis of the responses

The questions regarding demographic overview, current utilisation and clinical studies were analysed on a national level, while the question regarding future indications was analysed on a responder-by-responder level.

2.3.1. Demographic overview/national organization

The number of responses from each country was recorded, and the countries with a central BT registry were identified. The persons who identified themselves as responsible for BT in their country were documented, and their contact details recorded for future use.

Finally, the number of BT centres per million inhabitants [14] in each country was provided. In the case of multiple answers from a country, the maximum and minimum number of reported centres per million inhabitants were determined.

2.3.2. Current brachytherapy utilization

To gain an overview of the current practice of BT across Europe, the number of clinical indications in the respective country was extracted from the responses. Additionally, the number of countries offering BT for the various clinical indications was found. In case of varying answers from the responders in a given country, all indications indicated by at least one respondent were counted. This was done based on the assumption that respondents would not be aware of all indications treated in the given country. The number of countries performing the individual BT types (High-dose rate (HDR), Pulsed-dose rate (PDR), Low-dose Rate (LDR) or other) was also recorded.

2.3.3. Future utilisation of brachytherapy

The survey included a question on which clinical indications the responders foresee to be the most frequent ones in the future (Table 1). This question was analysed in two ways. Firstly, the total number of respondents (not accounting for nationality) identifying a given indication was determined. Secondly, it was investigated, if respondents answered an indication currently not performed in their country. Hence, for each respondent, the indications already mentioned as being performed in the country were ignored, and the total number of respondents for each of these remaining indications were determined. For instance, if a respondent reported “gynaecology” and “prostate” as being treated with BT, and then marked “gynaecology” and “skin” as the most frequent indications in the future, then in the second part of the analysis, only “skin” was counted. The latter was done, based on the assumption that if a respondent identifies an indication not currently performed in the country as the most frequent in the future, this indication might have a potential to be treated with BT in the future.

2.3.4. Clinical studies and trials

The number of countries currently conducting clinical studies was determined by counting all countries, where at least one respondent marked the given type of study to be conducted. Similar to the analysis of current utilisation of BT. The survey did not allow for investigation on whether the various studies were multinational. Hence, a single multinational trial might be counted twice and the actual number of studies and trials might be lower than presented here.

3. Results

Responses were received from 26 out of 37 (70 %) approached countries. Single responses were received from 15 countries. From eight countries, between two and five responses were received, from the last three countries >5 responses were received. A full overview over the responses from each country is given in the supplementary material (Tables S1–S3).

3.1. Demographic overview/national organization

The responding countries were almost equally divided between Eastern and Western Europe. In addition, replies were received from two countries outside Europe (Fig. 1). In the majority (20 out of 26) of the countries, at least one of the respondents acknowledged to be responsible for BT in the respective country. In three of these countries, multiple respondents acknowledged to be responsible. On the other hand, central registries for BT are not widely used, with at most 12 out of 26 countries reporting having one, with no obvious demographic bias (Northern, Eastern, Western or Southern Europe).

BT availability varied between countries from 0.4 BT centre per million inhabitants to 2.3 (Fig. 2). The number of centres were not reported in two countries, and in six countries, there was a variation in the number of centres reported by the responders. The smallest variation was a difference of one centre across the replies in the given country, while the largest variation was between 7 and 34 reported centres in a single country.

3.2. Current brachytherapy utilization

The number of clinical indications currently treated with BT varies widely from country to country. In one country, BT is no longer offered. In all other countries BT is used for gynaecological indications, while BT is used for prostate cancer in 88 % of the countries (Table 2). Six other indications are treated in about half of the countries, though not in the same countries. One of these is salvage after recurrence, which might be underreported, since such treatments might also be listed on the individual indications. On average, each country treated 5 different indications, but this varied from 0 to 13 (Fig. 2).

All countries offer HDR BT, while LDR treatments are used in 21 of the 26 countries. PDR BT on the other hand is only performed in half of the countries. Eight countries marked, the option “others”. Five of these performs eye plaque BT, two superficial or electronic BT, and the last one both eye plaque BT and superficial BT.

3.3. Future utilisation of brachytherapy

Gynaecological and prostate cancer were the most frequently identified indications for the future (Table 2). Salvage after recurrence, head and neck and sarcoma diagnosis were the indications most often identified as the most frequent in the future by respondents from countries were these indications are currently not being performed (Table 2).

3.4. Clinical studies and trials

Respondents from 15 different countries indicated ongoing studies or clinical trials in their country. This fits well with 19 of the countries

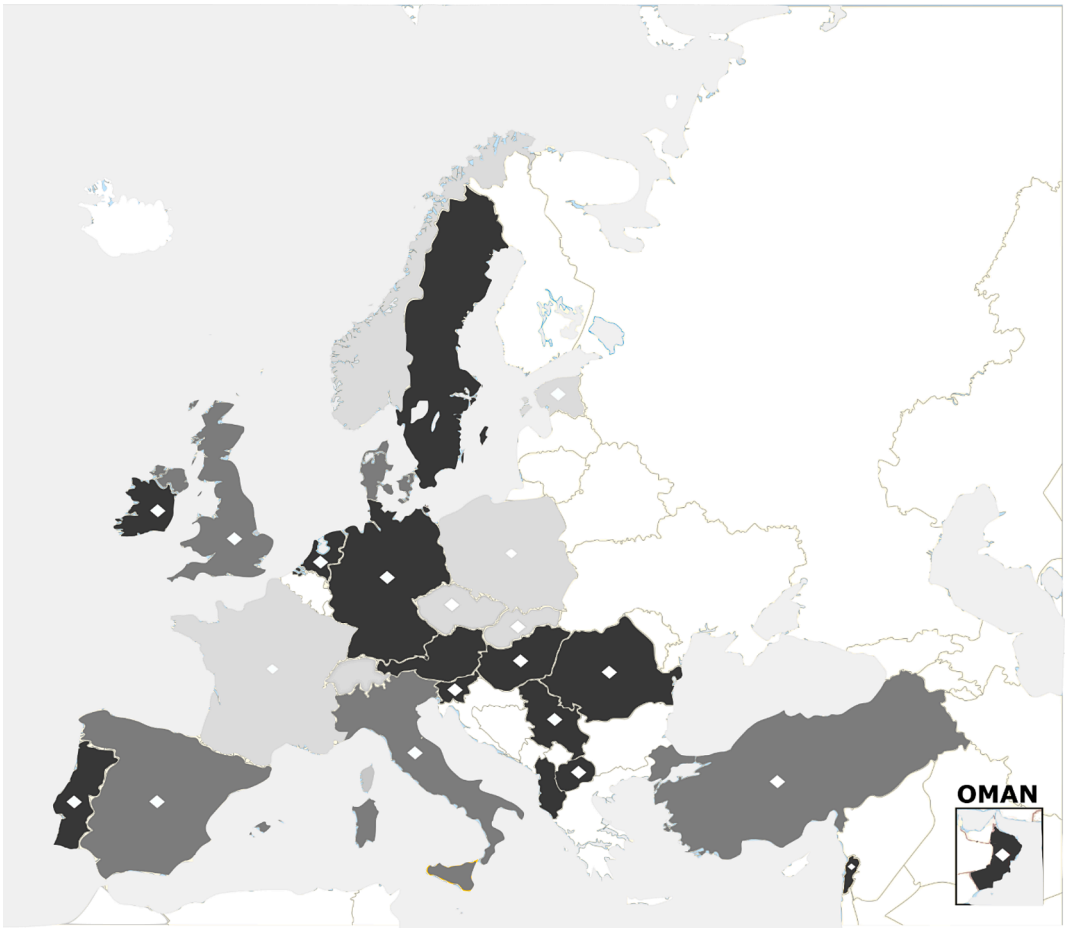


Fig. 1. A map showing the countries from which responses were received (white countries: no responses received). The colours indicate whether or not a national BT registry exists (Light grey: countries reported to have a registry, Black: Countries with no reported registry, dark grey: Both yes and no answers received from the given country regarding a national registry). Countries with at least one BT responsible person are indicated with a white diamond.

having registered active trials, and the trials are recruiting in 14 of the countries [15]. The types of studies range from prospective registries to phase III trials. In six countries, there are ongoing phase III trials, and in ten countries, there are ongoing phase II trials. Most of these trials are performed in Western Europe with only one Eastern European country performing a phase III trial and only two performing phase II trials.

4. Discussion

A short survey was distributed in May 2023 by the GEC-ESTRO Brachy-HERO group with the aim to provide pilot data for more in-depth studies. The few questions resulted in quick responses and a high response rate with 80 responses from all over Europe (and beyond) within two months. The answers showed a widespread use of BT for a few indications, mainly gynaecological sites and prostate cancer. Indications such as skin, eye and head and neck cancer are, however, also treated with BT in more than half of the responding countries. In general, BT seems to be an integrated part of radiotherapy in most European countries, but mainly as a specialised treatment for a few indications. This correlates well, with what has been previously reported based on interviews with BT experts [12]. The number of BT centres reported is approximately half of the number of external beam departments as reported by the ESTRO-HERO group, with a mean of 0.78 BT centre per million inhabitants relative to a mean of 1.7 departments per million inhabitants [13]. It should be noted that information about the number of afterloading machines per country was not collected. Thus, the number of centres reported in Fig. 2, is given instead of number of afterloading machines. Since a centre may have several afterloading machines, these numbers do therefore not necessarily indicate the capacity of BT in each country.

Overall, the responses from the survey give the impression that BT is a very decentralised modality with a limited number of countries having central registries and a significant number of countries having no central person responsible for BT related issues. This is also reflected in the large variation in the clinical indications between countries, and the large variations of answers within countries. The field could therefore benefit from greater collaborations between countries and clinics, also to ensure that all patients, which would benefit from BT, will receive it, regardless of their country of residence. An important part of ensuring consistent use of BT is evidence-based knowledge on the potential benefits. For this, it is encouraging to see that there are ongoing phase II and III trials in several countries. The survey only provided information on the countries with ongoing trials, and a more elaborate study of, which trials are currently ongoing (like clinical indications inclusion criteria, etc.), is needed.

The study is limited by the simplicity of the survey. A simple survey was chosen in the hope that this approach would increase the chance of receiving a high response rate in a short time. The limitation of this is that the data collected are rather limited and only provide overviews. Furthermore, in many countries, the national societies were not able to identify a single person with a clear overview over the brachytherapy utilisation in the country. Hence, the survey was broadly distributed to brachytherapy clinics. This led to multiple responses from some country. Responses that in some cases were contradicting. Indicating that the respondents did not have a full overview of the situation in the country. Hence, the absolute numbers are encumbered with a significant

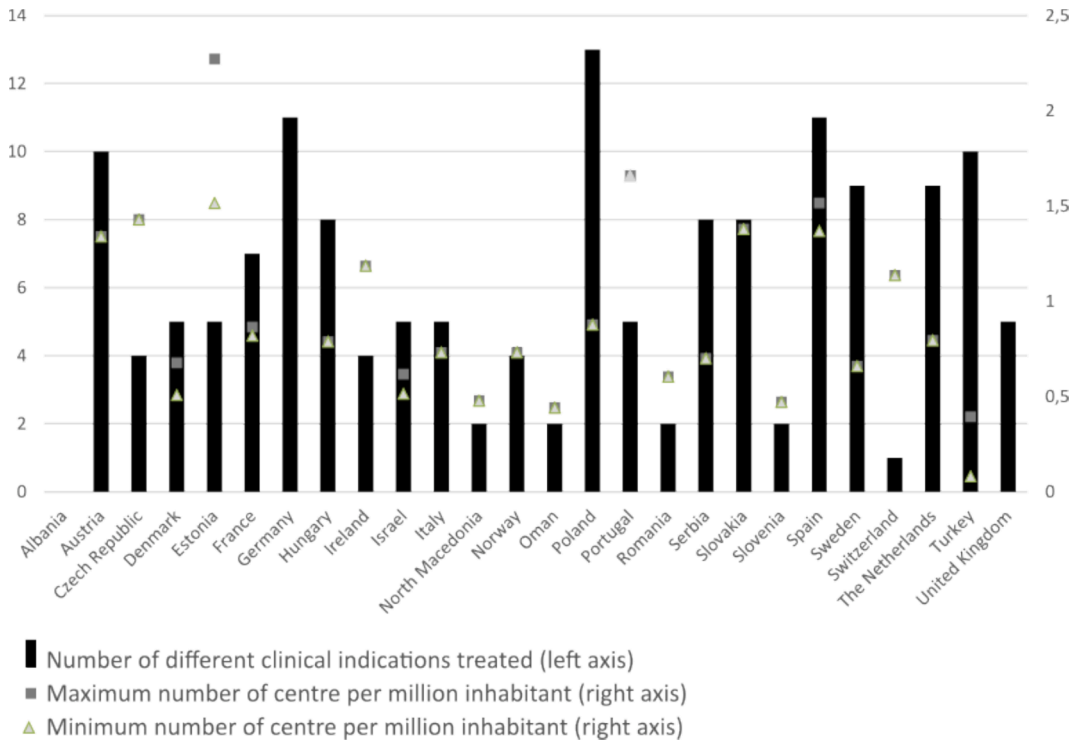


Fig. 2. The number of BT centres per million inhabitants (right-side y-axis). Both maximum (dark grey squares) and minimum (light grey triangles) reported number of centres are shown. Black bars: The amount of different clinical indications treated with BT in the given countries (left-side y-axis).

Table 2
Overview of the current and possible future utilisation of BT for different indication. The current practise is analysed on a national level (maximum 26), while the most frequent indications in the future are analysed on a responder level (maximum 80).

Clinical indication	Current practise Absolute number (%)	Most frequent indication in the future Absolute number (%)	Most frequent indication in the future, which is not reported as being performed in the country Absolute number (%)
Gynaecology	25 (96 %)	75 (94 %)	0 (0 %)
Prostate	23 (88 %)	50 (63 %)	13 (16 %)
Skin	15 (58 %)	36 (45 %)	8 (10 %)
H&N	14 (54 %)	18 (23 %)	10 (13 %)
Eye	14 (54 %)	16 (20 %)	3 (4 %)
Salvage after reccurence	13 (50 %)	29 (36 %)	14 (18 %)
Breast	11 (42 %)	25 (31 %)	9 (11 %)
GI	11 (42 %)	14 (18 %)	9 (11 %)
Sarcoma	7 (27 %)	16 (20 %)	10 (13 %)
Keloids	7 (27 %)	16 (20 %)	5 (6 %)
Lung	7 (27 %)	7 (9 %)	3 (4 %)
Paediatric	4 (15 %)	11 (14 %)	5 (6 %)
Liver	2 (8 %)	6 (8 %)	4 (5 %)
Other	2 (8 %)	0 (0 %)	0 (0 %)

uncertainty, but clear trends, such as the most frequent indications, were still seen in the data.

A strong motivation behind the survey was to identify elements affecting the utilisation of brachytherapy in Europe, and create a platform to perform more in-depth studies. Based on this survey, the plan is to investigate the types of ongoing trials and to investigate what causes the large variation in indications treated with brachytherapy from country to country.

In conclusion, BT continues to be included in cancer treatment in most European countries. The two main indications are gynaecological and prostate cancer treatment, but also other indications like skin and head and neck cancer are treated with BT in several countries. Also, in the future, gynaecological and prostate cancer were seen as the most important ones, but salvage after recurrence also scored high both in general and from respondents currently not performing I it.

CRediT authorship contribution statement

J.G. Johansen: Conceptualization, Formal analysis, Visualization, Writing – original draft. **I.M. Jürgenliemk-Schulz:** Conceptualization, Writing – review & editing. **H. Haddad:** Conceptualization, Writing – review & editing. **J.M. Hannoun-Levi:** Conceptualization, Writing – review & editing. **T.P. Hellebust:** Conceptualization, Writing – review & editing. **B. Guix:** Conceptualization, Writing – review & editing. **K. Loessl:** Conceptualization, Writing – review & editing. **B. Pieters:** Conceptualization, Writing – review & editing. **C. Rao:** Conceptualization, Writing – review & editing. **V. Strnad:** Conceptualization, Writing – review & editing. **A.E. Sturdza:** Conceptualization, Writing – review & editing. **L. Tagliaferri:** Conceptualization, Writing – review & editing. **Z. Takacsi-Nagy:** Conceptualization, Writing – review & editing. **E. Villafranca:** Conceptualization, Writing – review & editing. **P. Wojcieszek:** Conceptualization, Writing – review & editing. **A. Rembielak:** Conceptualization, Writing – review & editing. **P. Niehoff:** Project administration, Methodology, Conceptualization.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ctro.2024.100883.

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