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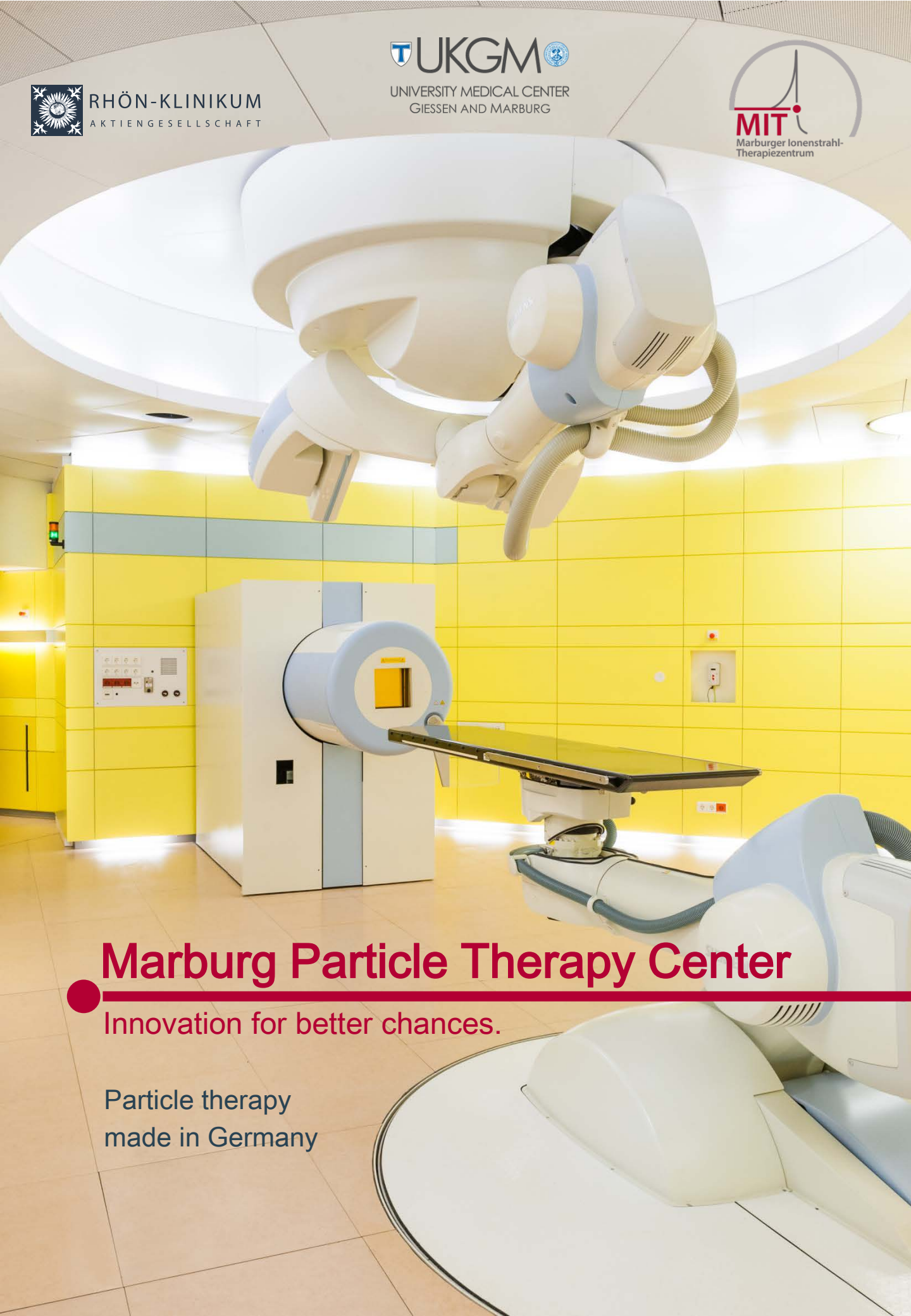
MIT
Marburger Ionenstrahl-Therapiezentrum



Marburg Particle Therapy Center

Innovation for better chances.

Particle therapy
made in Germany

Dear Colleagues,

You will certainly know situations where you alone are no longer able to provide adequate therapies for patients suffering from cancer characterized by an unfavorable location or biological and genetic properties that require highly precise and preserving treatment modalities.

During the last years, proton and heavy ion radiation could be established as good therapeutic option for some indications that may be applied alone or as an addition to photon therapy for the benefit of our patients.

The Marburg Particle Therapy Center (MIT) at the University Hospital of Giessen and Marburg is one of only two centers in Germany where also heavy ion radiation with carbon ions may be provided beside proton radiation.

In comparison to photon, but also proton radiation, the special feature of carbon ion therapy is the significantly higher biological effectiveness due to the much denser energy release to the irradiated tissue (so-called high-LET effect).

All patients who are referred to the MIT for treatment or combined therapy are presented and discussed in the context of interdisciplinary tumor boards with special focus on particle therapy.

Only if – together with you as treating physicians – an individual treatment benefit may be expected for the patients, we start planning proton or heavy ion radiation.

We do not only aim at making this highly innovative therapy accessible for your patients, but also at further developing it together with you. For this purpose, a relevant number of therapy trials are offered and conducted, in which nearly all patients are included.

Since the beginning of irradiation therapy at the MIT at the end of 2015, we could already help more than 800 patients. Often questions are asked like for example which patients might benefit from particle therapy, if it is possible to combine particle therapy with photon therapy performed near the place of the patient's residence, if statutory or private health insurances cover the expenses, which trials are conducted at the MIT, or how one may reach us.

With this booklet, we want to give you a brief "guide" to particle therapy in Marburg. We would be happy to make innovation available for our patients together with you.

We are looking forward to getting in contact with you. Of course we are available for individual consultation.

With best regards,

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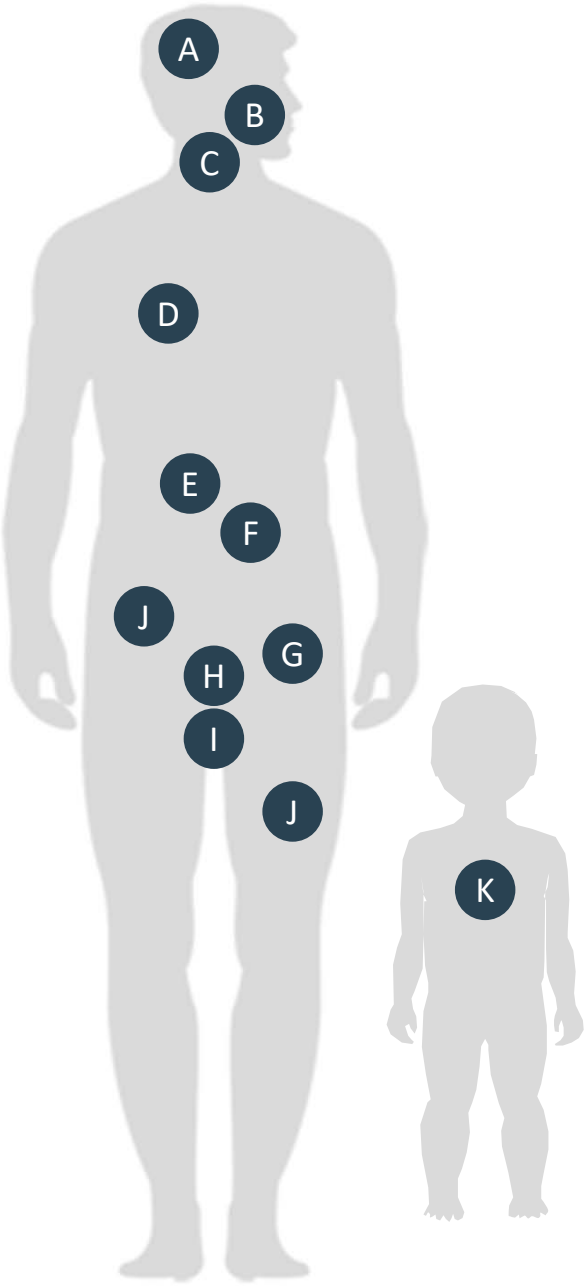
Indications to be treated at the MIT

Already today, more than 50% of all patients suffering from cancer may be healed. In this context, radiotherapy plays a significant role. In addition to photon therapy, particle therapy allows further radiotherapeutic options with even higher accuracy and effectiveness that is very promising with regard to increased healing rates and reduced side effects.

In particular tumors that are resistant to radiation in the neighborhood of critical risk structures or tumors beside organ structures that are highly sensitive to radiation exposure seem to be suitable for this therapy option.

Proven indications are chordomas and chondrosarcomas of the skull base as well as tumors of the salivary glands, especially adenoid-cystic carcinomas (ACC) and mucosal melanomas. Promising results have been observed in the treatment of carcinomas of the nasal cavity and the paranasal sinuses with organ preservation. Further indications may be certain types of pancreatic cancer, retroperitoneal sarcoma, and recurrences of the pelvic wall.

Particularly children benefit from the extremely high precision of protons. They allow significantly better preservation of the surrounding healthy tissue. Most frequently observed pediatric tumors treated at the MIT in the context of GPOH trials (International Society for Pediatric Oncology) are brain tumors, sarcomas, or Hodgkin lymphomas. Infants undergo radiotherapy under general anesthesia.



- **A** Malignant and benign brain tumors
- **B** Head and neck tumors
- **C** Tumors of the salivary glands
- **D** Lung tumors
- **E** Liver cancer
- **F** Pancreatic cancer
- **G** Recurrences of the pelvic wall
- **H** Prostate cancer
- **I** Recurrences of rectal carcinomas
- **J** Sarcomas
- **K** Pediatric tumors

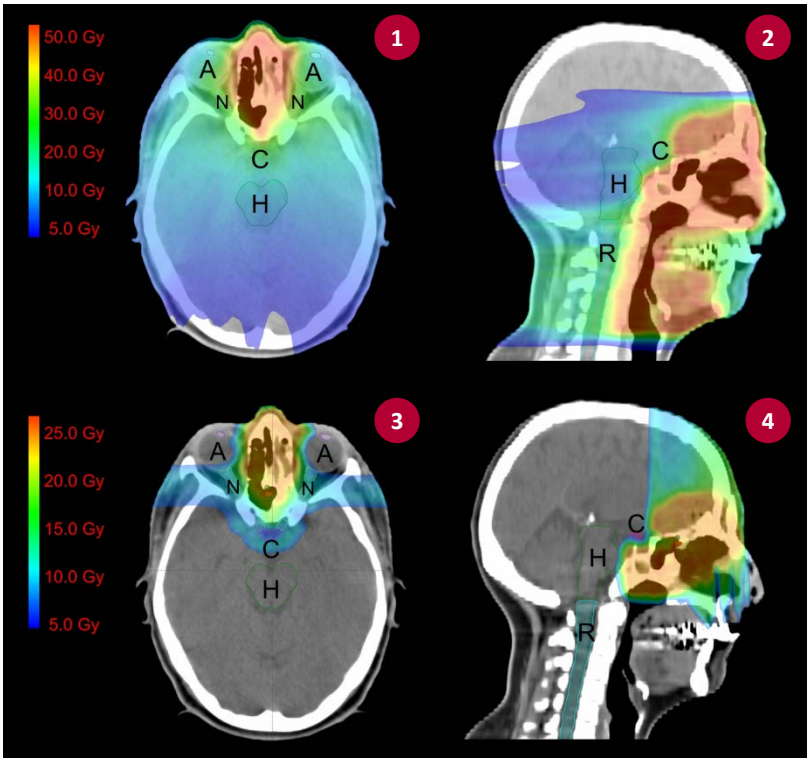
Therapy of primary indications and recurrences: Treatment indications

Particle therapy may be performed with curative intention alone, but also as boost to photon therapy as well as combined therapy with surgery or drug-related therapy.

The following indications are currently approved by the German Federal Joint Committee (Gemeinsamer Bundesausschuss, G-BA) and treated at the MIT in the context of prospective study protocols:

 **Head**	• **Glioblastomas, gliomas WHO III°, low-grade gliomas** • **Meningiomas** • **Pituitary adenomas** • **Craniopharyngiomas** • **Esthesioneuroblastomas, acoustic neuromas, vestibular schwannomas, glomus tumors, recurrences** • **Cerebral arteriovenous malformations (AVM)** • **Skull base tumors**
 **ENT**	• **Tumors of the head and neck, especially nasal cavity and paranasal sinuses with organ preservation** • **Carcinomas of the salivary glands, especially adenoid-cystic carcinomas (ACC)** • **Carcinomas of the nasopharynx** • **Local recurrences**
 **Thorax**	• **Lung cancer** • **Pancoast tumors** • **Esopharyngeal carcinomas** • **Hodgkin tumors of the mediastinum**
 **Abdomen**	• **Retroperitoneal sarcomas** • **Pancreatic cancer**
 **Pelvis**	• **Prostate cancer** • **Recurrences of the pelvic wall** • **Recurrences of rectal carcinomas**
 **Sarcomas**	• **Paraspinal sarcomas/carcinomas** • **Chordomas** • **Chondrosarcomas** • **Osteosarcomas** • **Soft-tissue sarcomas**
 **Pediatric tumors**	• **Ependymomas** • **Retinoblastomas** • **Medulloblastomas** • **Gliomas** • **Lymphomas** • **Sarcomas** • **Neuroblastomas** • **Germ cell tumors** • **Craniopharyngeomas**

Boost therapy: photons and particle therapy may well complement each other



Dose distribution of the photon ground (❶❷) as well as carbon ion boost plan (❸❹) for a locally advanced carcinoma in the area of the paranasal sinuses. By using carbon ions for dose increase in the area of the primary tumor, it is possible to preserve important risk structures and at the same time optimize the radiation effect on the tumor.

A – eye
N – optic nerve
R – spinal cord/medulla
C – optic chiasma
H – brainstem

Beside irradiation alone that includes particle therapy at the MIT in Marburg, there are several other indications allowing the application of particle therapy in combination with photon therapy.

In the context of boost therapy, first the high-risk region is treated in 5 to 10 fractions with protons or carbon ions at the MIT in Marburg.

Afterwards, photon therapy is performed near the patient‘s residence in about further 25 sessions of intensity-modulated application. For this purpose, you will receive a digital version of the target volume and the radiation plan in DICOM format.

With boost therapy, you as treating physicians have the possibility to effectively enlarge your therapeutic approach with particle therapy for suitable patients.

The costs for particle therapy and photon therapy are charged independently from each other to the statutory and private health insurances.

The following indications are suitable for combined treatment with photon and particle therapy at the MIT in the sense of boost therapy:

- **Glioblastomas, gliomas WHO III°**
- **Carcinomas of the nasal cavity and the paranasal sinuses**
- **Mucosal melanomas of the nasal cavity**
- **Carcinomas of the nasopharynx**
- **Carcinomas of the salivary glands**
- **Advanced tumors of the head and neck**
- **Non-resectable esophageal carcinomas**
- **Prostate cancer**

Frequently asked questions

What is the difference between particle therapy and photon therapy?	Photon therapy consists of irradiating the target area with gamma rays; in the context of particle therapy, radiation is performed with protons and heavy ions (mainly C12 carbon ions). Both types of radiation lead to DNA damage of the tumor cells in the target area. Only if the cells are no longer able to repair this damage, this leads to cell death and thus to deletion of the tumor. The degree of the DNA damage depends relevantly from the radiation dose. Due to the physical properties (precision), a significantly higher radiation dose can be applied to the target area in cases of particle therapy compared to photon radiation, with preservation of the surrounding tissue. The dose reaching the tissue behind the tumor decreases to nearly 0 Gy so that healthy tissue is not involved. Since carbon ions cause significantly severer DNA damage compared to protons and photons, they are most frequently applied in cases of tumor entities that are resistant to radiation. According to the individual needs, both options of particle radiation may be chosen at MIT.
Which patients may benefit from particle therapy?	The cells of some tumor entities are resistant against photon radiation. Also regarding tumors that are located deeply in the body or beside very sensitive tissues or organs, like for example brainstem, optic nerve, heart, or intestine, intensity-modulated radiotherapy reaches its limits. This means that an effective target dose can only be applied if the patient accepts that the surrounding tissue is damaged or alternatively the tumor is underdosed. In these cases, particle therapy is a significantly superior radiation alternative. Due to its physical properties and the biological efficacy spectrum, high radiation doses may be applied in relatively deep body regions by means of proton or heavy ion radiation with preservation of the surrounding tissue.
Why do especially pediatric patients benefit from proton therapy?	The main advantage for children results from the above-mentioned biological and physical properties of the radiation beam. This is particularly important for pediatric patients since long-term side effects such as growth and developmental deficits may be avoided.
How can I present and refer my patients to the MIT?	You may either submit your enquiry regarding particle therapy at Marburg or Giessen by e-mail (partikeltherapie@uk-gm.de), by mail (Strahlentherapie UKGM Marburg, Baldingerstr., 35043 Marburg, Germany), or by calling +49-(0) 6421-58 63974.

Is there a central contact for the patients?	The central contact points for your patients are our specialist consultancies for particle therapy in the Department of Radiotherapy and Radiooncology at the University Hospital of Giessen and Marburg. For appointments, please call us (+49-(0) 6421-58 63974 or write an e-mail to partikeltherapie@uk-gm.de.
Which documents will be required?	The following documents (if available) will be required for registration: • Medical report describing the stage, course, and current symptoms • Recent diagnostic imaging (digital format, e.g. CD) with current and previous findings (if available) • Histology • In cases of previous irradiation: documentation of the radiation exposure (please submit a digital radiation plan in DICOM format and a printed version of the radiation protocol) • Referral letter and health insurance card
Do statutory and private health insurances cover the costs for particle therapy?	In general, the statutory and private health insurances cover the expenses of particle therapy. Similar to all therapeutic innovations in the healthcare system, they are not automatically integrated in the standard care catalogue. So it is necessary to previously apply for cost coverage. Meanwhile, we were able to establish specific contracts with many statutory health insurances for the majority of our patients so that cost coverage is usually possible without any problem in the context of indications mentioned in this booklet. Regarding other statutory or private health insurances, we conclude individual agreements.
Which trials are conducted or planned at the MIT?	In cooperation with the German Society of Radiooncology (Deutsche Gesellschaft für Radioonkologie; DEGRO) and the Federal Joint Committee (Gemeinsamer Bundesausschuss, G-BA), a list of tumor diseases was elaborated that might be suitable for particle therapy. These tumor diseases are treated in the context of prospective trials or randomized clinical protocols. For detailed information, please visit www.ukgm.de/mit
What about follow-up after particle therapy?	After completed particle therapy, in most cases the first follow-up examination is performed in our outpatient department, if needed imaging is performed. Afterwards we provide regular radiotherapeutic follow-up up to 5 years after therapy, which is also performed in cooperation with the responsible oncologist of the respective discipline, similar to follow-up after photon therapy. If the patients or the referring radiotherapists desire, the follow-up examinations after the second interval may also be performed near the patients' residence.

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Imprint

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