Beyond two rooms: proton therapy access for all

Philip Blumenfeld MD MPH and Aron Popovtzer MD

Sharett Institute of Oncology, Hadassah Medical Center, Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem, Israel

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Israel is approaching a pivotal moment in the development of its radiotherapy infrastructure. Demand for advanced radiation technologies continues to grow as the incidence of cancer rises and survival improves, placing increasing pressure on an already stretched oncology system. National planning efforts have identified the establishment of a national proton therapy center as part of Israel's future radiotherapy infrastructure [1]. The central question is no longer whether proton therapy should exist in Israel, but rather how it should be implemented. Specifically, will national infrastructure be designed to ensure equitable clinical access and meet future demand, or will it reflect the historically limited utilization that resulted from the need to send patients abroad for treatment?

Proton therapy offers clear physical advantages over conventional photon radiotherapy. By exploiting the Bragg peak, protons deposit the majority of radiation dose at a defined depth with minimal exit dose beyond the target. This procedure allows improved sparing of surrounding normal tissues and critical organs [2]. In selected clinical settings these dosimetric advantages translate into meaningful reductions in both acute and long-term toxicity.

Over the past decade proton therapy has expanded rapidly. The Particle Therapy Co-Operative Group now tracks more than 120 proton therapy facilities operating globally, with additional centers under development across Europe, North America, and Asia [3]. As clinical experience has accumulated, the evidence supporting proton therapy has also matured. Comparative effectiveness research suggests that proton therapy can reduce treatment-related toxicity while maintaining comparable oncologic outcomes. In one large cohort of patients receiving concurrent chemoradiotherapy, proton therapy reduced severe grade 3 or higher adverse events requiring hospitalization from 28% to 12% while maintaining similar disease control [4].

Proton therapy is already considered standard treatment for several malignancies, including pediatric cancers, ocular melanomas, chordomas, and chondrosarcomas [2]. In pediatric brain tumors, systematic reviews demonstrate significant reductions in long-term toxicities such as endocrine dysfunction and neurocognitive decline without compromising tumor control [5]. Beyond these established indications, a growing body of comparative clinical and dosimetric evidence suggests potential advantages across additional disease sites including head and neck cancers, mediastinal lymphoma, thoracic malignancies, liver tumors, and reirradiation scenarios where limiting cumulative radiation dose to previously treated organs is particularly important [6-10]. Major clinical indications and the rationale supporting proton therapy are summarized in Table 1. These developments reflect a broader shift in oncology toward treatments that maintain oncologic efficacy while minimizing long-term toxicity. As survival improves and patients live longer after treatment, reducing treatment-related complications becomes increasingly important.

CAPACITY IS THE FIRST PILLAR

Estimating national demand for proton therapy is essential for rational healthcare planning. National data on radiotherapy volumes in Israel are not fully published, but reasonable estimates suggest that approximately 25,000–30,000 patients receive radiotherapy annually, including both definitive and palliative treatments. Even with conservative estimates of clinical indication, proton candidates are not negligible. Modeling studies suggest that approximately 5–13% of radiotherapy patients may substantially benefit from proton therapy, with a commonly cited estimate near 13% and a secure lower bound of approximately 4.3% [11,12]. Under these assumptions, the number of patients who could potentially benefit from proton therapy in Israel ranges from roughly 1250 to 3900 patients per year.

Table 1. Major clinical and expanding indications for proton therapy

Indication	Key rationale
Pediatric malignancies	Reduces dose to developing tissues, lowering risks of neurocognitive, endocrine, growth, and secondary malignancy effects
Central nervous system tumors	Limits dose to normal brain and critical structures; may reduce late neurocognitive and endocrine toxicity
Ocular melanoma	Highly conformal treatment with eye preservation
Skull base tumors	Enables dose escalation near critical structures
Head and neck cancers	Reduces radiation exposure to salivary glands, swallowing structures, potentially reducing treatment-related toxicity
Mediastinal lymphoma	Significantly lowers radiation exposure to the heart, coronary arteries, lungs, and breast tissue
Thoracic malignancies	Reduces radiation dose to critical cardiopulmonary structures including heart and lungs while maintaining tumor coverage
Breast cancer	Reduces cardiac irradiation and contralateral breast dose in select cases
Liver tumors	Spares uninvolved liver and adjacent gastrointestinal organs
Sarcomas	Facilitates dose escalation for radioresistant tumors
Reirradiation	Reduces cumulative dose to previously irradiated tissues

By comparison, a two-room proton therapy center treating 250–400 patients per room annually would treat approximately 500–800 patients per year. Even under the lowest-demand scenario of 5%, two rooms would cover only about 40–50% of potential need. Under more realistic scenarios of 10–13%, coverage falls to approximately 20–30% or less. In other words, two treatment rooms are unlikely to meet national demand if access expands even modestly beyond the minimum estimate. Published planning studies reinforce this conclusion. Modeling of proton therapy capacity suggests that approximately 270 patients per treatment room annually represents a realistic operational throughput, with a theoretical maximum of roughly 400 depending on fractionation schedules and operating hours [13]. These estimates highlight the potential gap between national need and the capacity of a limited number of treatment rooms. The arithmetic therefore highlights a fundamental planning issue: national need is likely to exceed the capacity of a single two-room facility.

ACCESS IS THE SECOND PILLAR

Radiotherapy treatments are delivered in daily fractions over several weeks, requiring repeated travel to treatment facilities. Concentrating proton therapy capacity in a single location therefore creates substantial logistical and financial burdens for patients who live far from that center. Even in a geographically small country such as Israel, daily travel for several weeks can impose significant hardship on patients and their families.

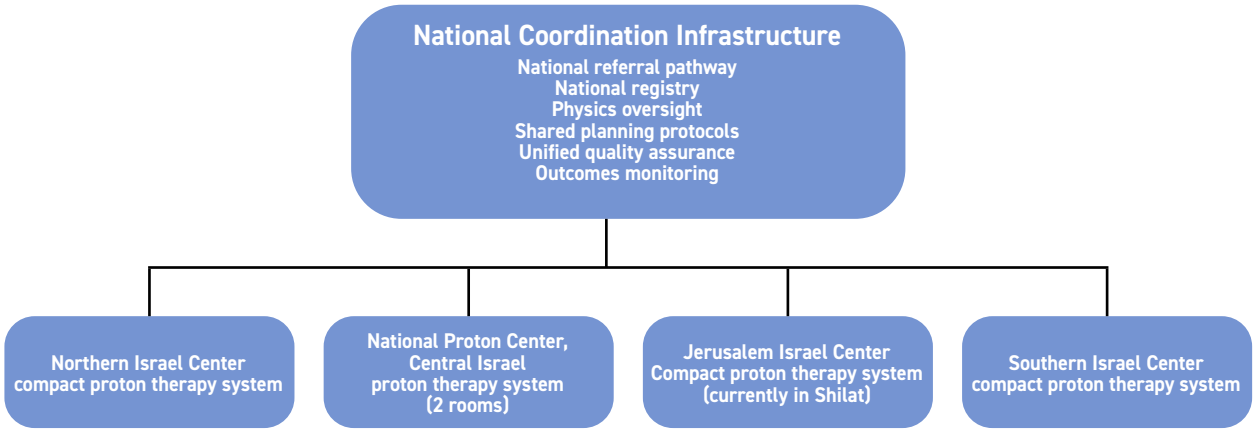
Geographic access is a well-recognized determinant of whether patients are able to receive proton therapy. A recent geospatial analysis demonstrated that only 36.6% of the population lives within a one-hour drive of a proton therapy facility, while more than 16% would require travel times exceeding 4 hours to reach treatment. Rural populations were more than twice as likely to face these extended travel times [14]. Because proton therapy typically requires daily treatments over multiple weeks, these distances translate into substantial logistical and financial barriers for patients and their families.

Even when treatment remains technically available, families may face cumulative burdens including lost workdays, travel expenses, temporary relocation during therapy, and disruptions to daily life. These challenges are particularly significant for pediatric patients and their caregivers, who often require prolonged treatment courses and extended family support. A distributed model incorporating centers throughout Israel would substantially reduce these barriers and allow more patients to receive treatment closer to home.

RESILIENCE IS THE THIRD PILLAR

A system based on a single facility also represents a single point of failure. If a two-room national center experiences maintenance interruptions, staffing shortages, or operational disruptions, proton therapy access for the entire country could be affected. Distributed infrastructure improves system resilience by reducing dependence on a single site. Multiple treatment locations allow patients to receive therapy closer to home while maintaining consistent national standards of care through shared clinical protocols and quality assurance.

Figure 1. Conceptual national network model for proton therapy in Israel combining the planned national center with distributed compact single room installations and shared national governance



Technological advances now make this approach increasingly feasible. Modern compact and gantry-less proton systems significantly reduce the infrastructure requirements of proton therapy compared with traditional multi-room facilities [12,15]. These platforms can operate within existing radiation oncology departments and require substantially smaller treatment vaults.

Israel has already demonstrated the feasibility of this approach. A compact gantry-less proton therapy system is already operational in the country, providing early clinical experience and demonstrating that modern proton platforms can be successfully integrated into Israel's healthcare infrastructure [15]. Early prospective clinical work evaluating upright image-guided adaptive proton therapy using this platform has demonstrated feasibility and safety in selected patients with recurrent head and neck and brain malignancies as well as thoracic tumors [16,17]. Rather than serving merely as a bridge until a national center is completed, this system represents the first operational node of proton therapy infrastructure in Israel.

TOWARD A NATIONAL PROTON THERAPY NETWORK

Israel therefore could develop proton therapy as a coordinated national network rather than a single institution [Figure 1]. The first phase should focus on establishing national governance infrastructure while building on the existing operational compact proton system. The second phase would include completion of the planned two-room national proton center, providing additional treatment capacity within the same coordinated national framework.

Subsequent phases could incorporate additional single-room compact proton installations in northern and southern Israel, integrated within existing oncology centers. A distributed system of approximately four treatment rooms nationally could treat roughly 1000–1400 patients annually while substantially improving geographic access. Shared planning protocols, national registries, and unified quality assurance standards could maintain consistent treatment quality across the network.

LOOKING FORWARD

The value of proton therapy lies not simply in technological sophistication but also in its ability to reduce treatment toxicity while maintaining excellent oncologic outcomes. Israel now has the opportunity to design a proton therapy strategy that reflects both clinical evidence and geographic realities. By building a coordinated national network that combines centralized planning with distributed access, Israel can ensure that proton therapy becomes an accessible national resource rather than a limited specialty service. In doing so, the country could also provide an international example of how emerging proton technologies can be integrated thoughtfully into a modern national healthcare system.

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Aron Popovtzer declares holding options in P-Cure Ltd.

Correspondence

Dr. P. Blumenfeld
Sharett Institute of Oncology, Hadassah Medical Center, Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem 9112001, Israel
Phone: (972-2) 677-6810
Email: philipb@hadassah.org.il

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There are none so sour as those who are sweet to order.

Luc de Clapiers, Marquis de Vauvenargues (1715–1747), French writer and moralist

Capsule

Re-administration of AAV-mediated gene therapy for OTOF-related deafness: a single-arm trial

Mutations in the *OTOF* gene are a major cause of congenital autosomal recessive deafness (DFNB9), which results from impaired synaptic transmission between inner hair cells and auditory neurons. Recent clinical studies have demonstrated that adeno-associated virus (AAV)-mediated *OTOF* gene replacement can partially restore hearing. However, the durability of treatment and the feasibility of re-administration have remained uncertain because of concerns regarding immune responses to viral vectors. In this single-arm clinical trial, **Fan** and colleagues evaluated the safety and efficacy of repeat AAV-mediated gene therapy in patients with *OTOF*-related hearing loss who required additional treatment after their initial intervention. Patients underwent a second administration of the therapeutic AAV vector and were followed for hearing outcomes and adverse events. The repeat treatment was well tolerated, with no serious treatment-related adverse events or evidence of clinically significant immune-mediated toxicity. Audiological assessments demonstrated further improvements in hearing thresholds, auditory brainstem responses, speech perception, and sound localization in several participants following re-administration. These findings indicate that the cochlea remains amenable to additional gene delivery and that repeated dosing can provide incremental functional benefits.

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