9th Annual Loma Linda Workshop on Particle Imaging and Radiation Treatment Planning

Innovative Developments in Spot Scanning Proton Therapy and Motion Management

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Research for a Life without Cancer

Agenda

1. **Commissioning of Novel Gantry-Less Proton Therapy System**
2. Motion Management: Optical Respiratory Monitoring

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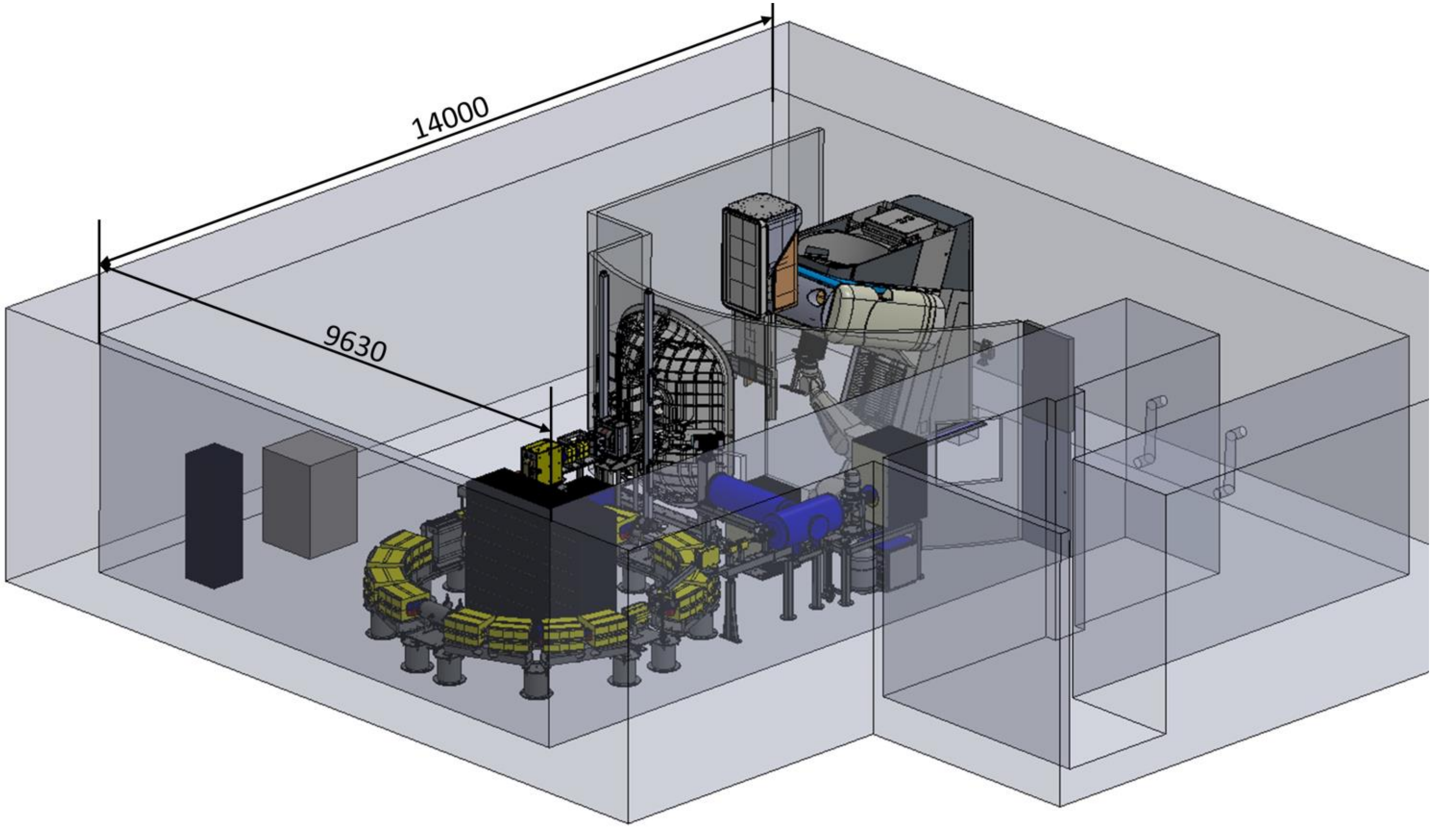
Location and timeline

- 2018: Start of accelerator component fabrication
- 2019: Accelerator assembly and physical launch (4 months)
- 2019 – 2020: Patient positioning and imaging system assembly and testing
- 2021: Approval from local (Israeli) authorities to use radiation mode
- 2022: Facility final tuning and commissioning
- 2023: FDA approval
- 2023, March 31: first patient

Single room compact synchrotron-based facility



Synchrotron Main Parameters

Energies for treatment, MeV	70 - 250
Intensity of extracted beam, p/s	2×10^9
$D_{synchrotron}$, m	5
$M_{accelerator}$, tons	15
Average energy consumption, kW	30

Synchrotron Main Components

- 16 bending magnets up to 1.9 T
- 16 horizontal and 4 vertical electromagnetic correctors
- 4 right gaps
- 1 RF station up to 15 MHz
- 1 electrostatic deflector up to 100 kV
- 8 BPMs
- 1 beam current sensor and 4 luminophores

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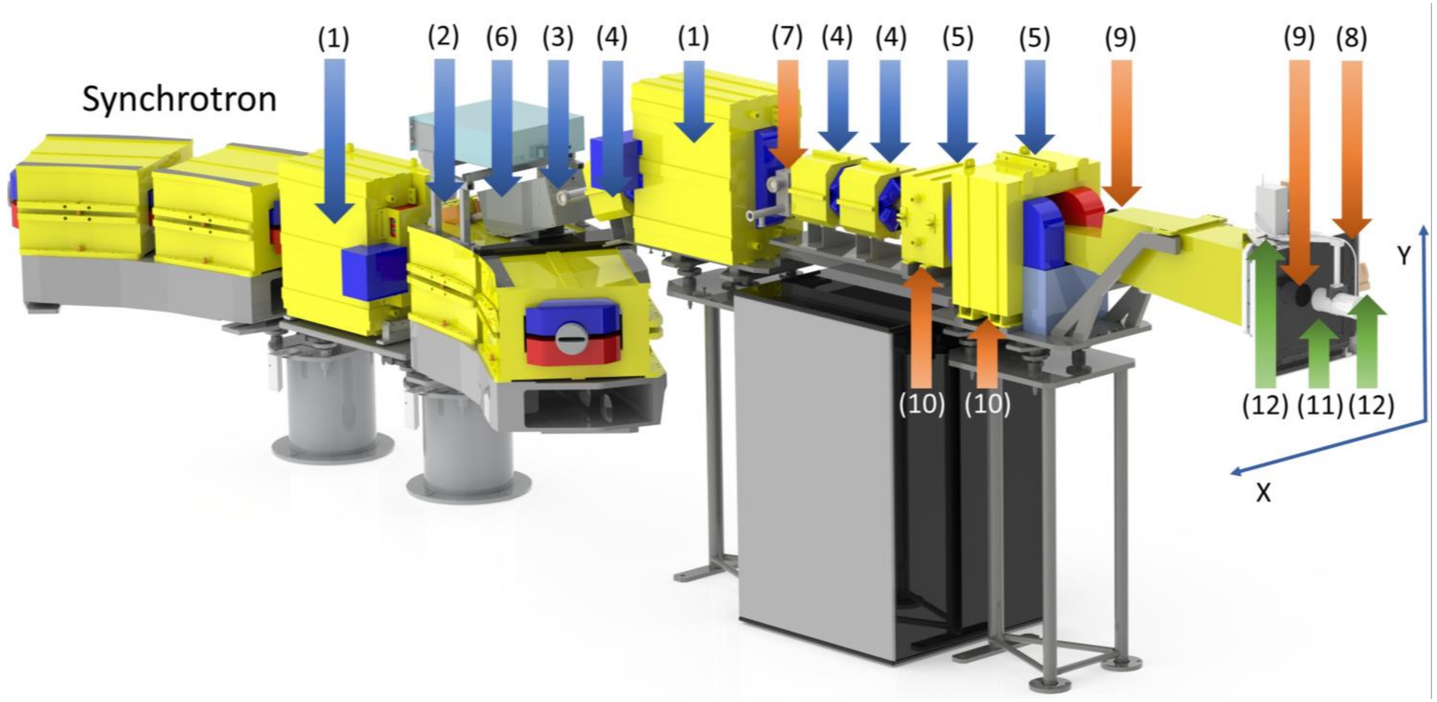
Beam delivery system



External devices

11. Removable Faraday cup
12. Lasers

1. Vertical electromagnetic correctors
2. Horizontal electromagnetic corrector
3. Beam control module (BCM)
4. Focusing quadrupoles
5. Scanning magnets
6. Fast magnetic shutter (FMS)

Dose Monitoring System (DMS)

7. Film based particle counter
8. ionization chamber IC128 by Pyramid Technical Consultants
9. Video camera-based beam position detector
10. Magnet-based beam position detector

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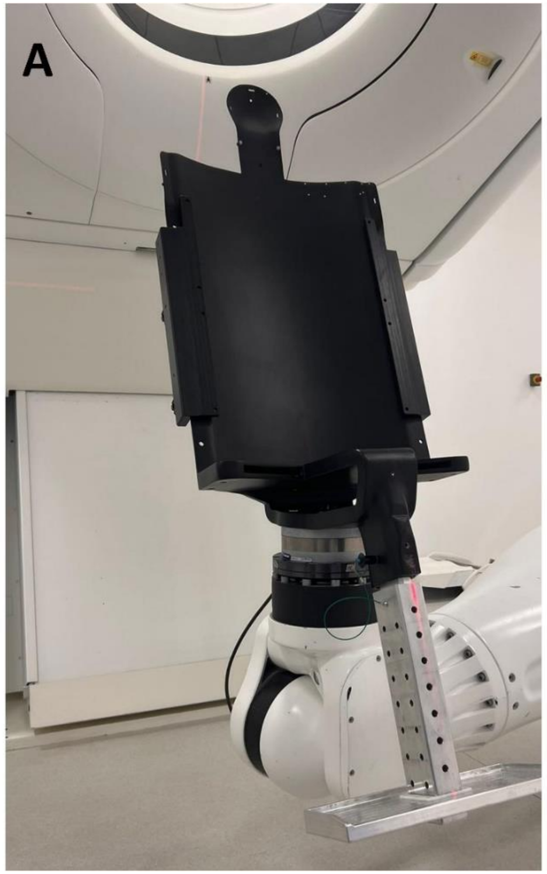
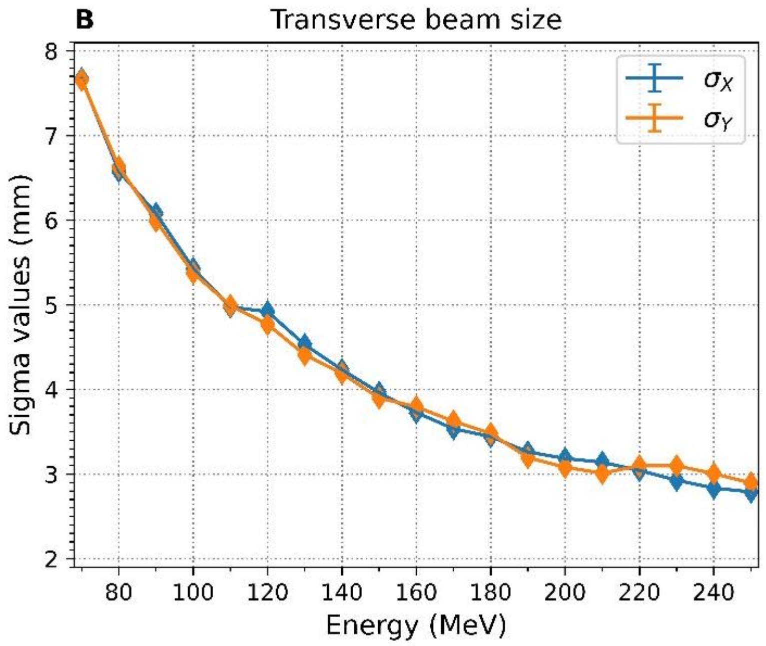
PAtient Robotic posiTioning and Imaging System (P-ARTIS)



Beam spot profiles



Distance, cm / Energy, MeV	45		55		70		85		100	
	σ_x	σ_y	σ_x	σ_y	σ_x	σ_y	σ_x	σ_y	σ_x	σ_y
70	6.16±0.08	6.06±0.08	6.73±0.07	6.66±0.07	7.67±0.04	7.66±0.04	8.71±0.05	8.76±0.05	9.77±0.06	9.87±0.06
100	4.30±0.07	4.16±0.07	4.71±0.06	4.61±0.06	5.43±0.04	5.38±0.04	6.17±0.03	6.16±0.03	6.92±0.04	7.01±0.04
150	3.21±0.07	3.07±0.07	3.49±0.05	3.39±0.05	3.96±0.03	3.90±0.03	4.46±0.01	4.46±0.01	4.99±0.02	5.03±0.02
200	2.60±0.07	2.47±0.07	2.81±0.06	2.69±0.06	3.18±0.05	3.08±0.05	3.53±0.03	3.49±0.03	3.97±0.03	3.95±0.03
250	2.34±0.06	2.44±0.06	2.5±0.1	2.7±0.1	2.79±0.09	2.89±0.09	3.1±0.1	3.2±0.1	3.5±0.2	3.7±0.2

Spot positioning and profile were evaluated using independent devices, including the built-in positioning sensors, the IBA Lynx, and Gafchromic EBT3 films. Spot positioning reproducibility was consistent within ±1 mm

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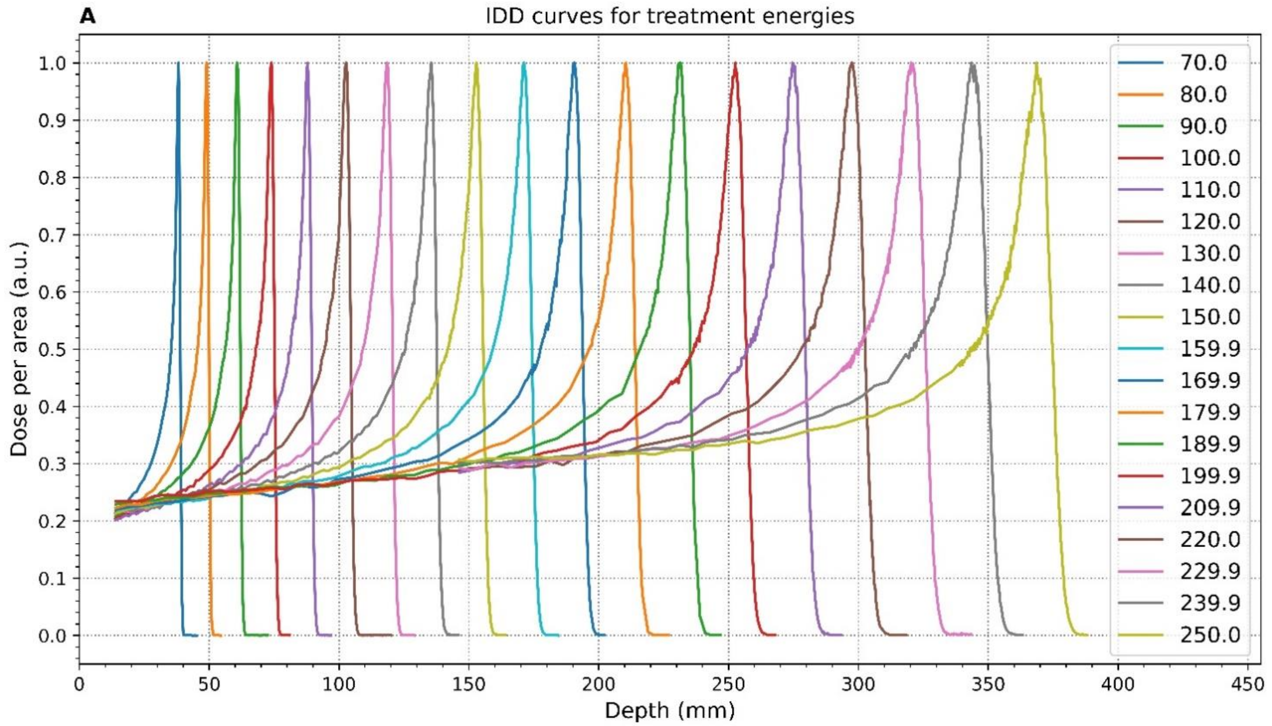
IDDs and absolute dose values



Energy accuracy was ±0.1 MeV

Distal R_{90} values reproducibility were within ±0.1 mm

- Ionization chambers (PTW Bragg Peak Chamber 34070/34080, Roos 34001) and a PTW MP3 water tank were used.
- The total amount of protons was 1.681×10^{11} per plan.
- TRS-398 coefficients:

$$0.999 \leq K_s \leq 1.019$$

$$0.993 \leq K_{pol} \leq 1.010$$

$$1.015 \leq K_{TP} \leq 1.019$$

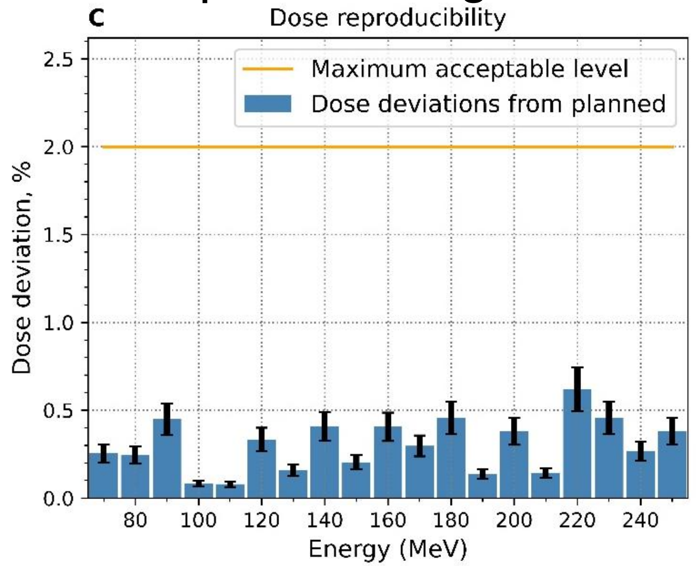
$$1.000 \leq K_{QQ0} \leq 1.002$$

- The maximum deviation between measured and planned dose was less than 0.6%

Treatment planning validation

Treatment scenario	Encompassing field size (cm^2)	Field #	Gamma index (3%, 3 mm)		
			Repetition 1	Repetition 2	Repetition 3
Clivus	4 × 5	1	100	100	100
	4 × 5	2	100	100	100
Bilateral neck	13 × 11	1	98.4	97.9	98.4
	11 × 11	2	100	100	99.3
	11 × 11	3	97.0	97.6	97.6
	13 × 11	4	99	96.5	96
Parietal	7 × 7	1	100	98.9	100
	7 × 7	2	100	100	100
Nasopharynx	5 × 7	1	100	100	100
	7 × 9	2	95.3	95.9	97.9
	7 × 9	3	100	100	100
Esophagus	8 × 10	1	95.4	95.4	96.2
	8 × 12	2	95.2	95.2	96
	8 × 11	3	97.3	95.6	98.3
Mediastinum	7 × 10	1	100	98.8	100
	7 × 10	2	96.3	95.1	98.8
Right chest wall	7 × 9	1	100	100	100
	7 × 9	2	100	100	100
Left upper lobe	9 × 7	1	100	100	100
	9 × 7	2	100	100	100
	9 × 7	3	100	100	100

- RayStation version 10B (RaySearch Laboratories AB, Stockholm, Sweden) was used for treatment planning.
- IBA MatriXX was used.
- The results of gamma analysis (3%, 3 mm) demonstrated pass rates greater than 95%.



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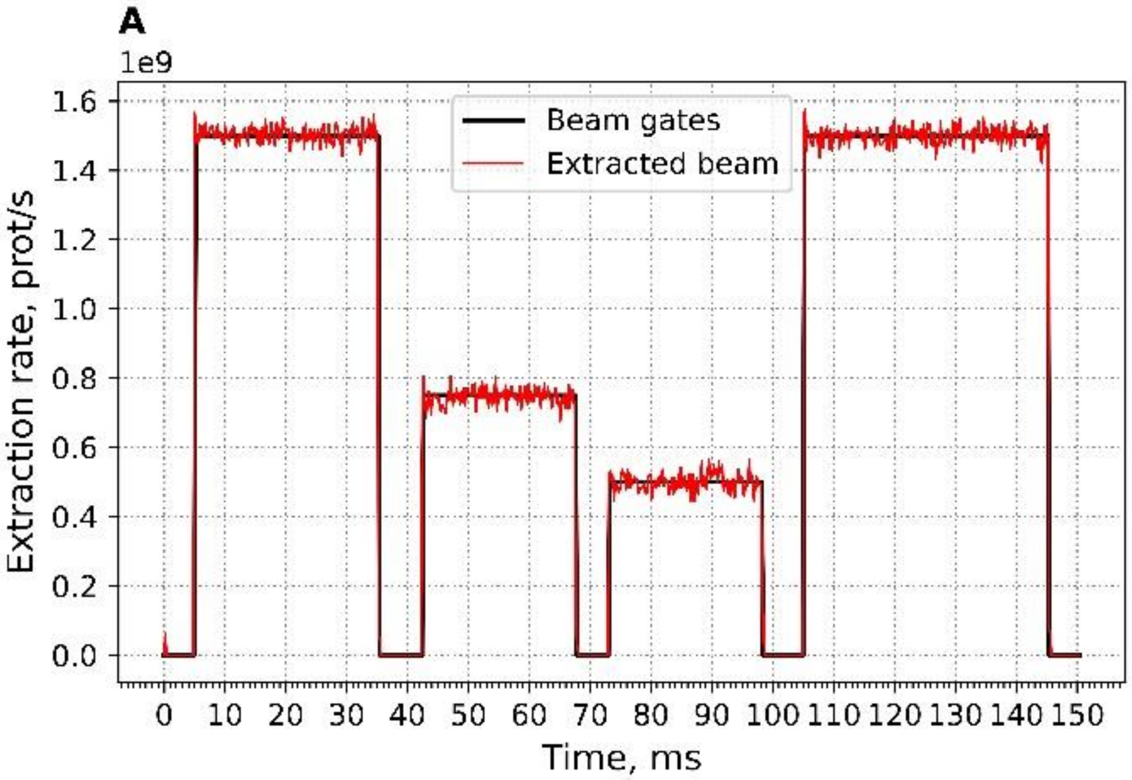
Extracted beam time structure



- The minimum planned spot length and the time between two consecutive spots are both 5 ms.
- The technical limit for spot length is 0.6 ms.
- Extraction rates:
- 7.3×10^8 protons/second @ 70 MeV
- 2.4×10^9 protons/second @ 250 MeV

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Clinical workflow demonstration

Ultra-low intensity extraction mode for proton radiography and CT

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BIOPHYSICS AND MEDICAL PHYSICS

Optimization of the Low-Intensity Beam Extraction Mode at the Medical Synchrotron for Application in Proton Radiography and Tomography

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Abstract—Proton therapy is one of the rapidly developing types of radiation therapy for oncological diseases. The use of proton imaging, a method in which the relative stopping power for protons is reconstructed directly, can significantly increase the accuracy and effectiveness of the proton therapy. This paper demonstrates the results of experimental work that was carried out at the synchrotron of the Prometheus proton therapy complex. The optimization of the synchrotron operating mode with low-intensity beam extraction was done for proton radiography and tomography purposes. Data about key changes of the beam extraction parameters for low-particles flux, as well as low-intensity beam control methods, are described.

Keywords: proton therapy, proton tomography, proton radiography, medical accelerators, proton synchrotron

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PAPER • OPEN ACCESS

Low Intensity Beam Extraction Mode on the Protom Synchrotron for Proton Radiography Implementation

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Article PDF

Commissioning Conclusions

- A novel single-room compact synchrotron-based gantry-less proton therapy facility was successfully commissioned.
- After commissioning, the facility began treating patients on March 31, 2023. It is the first proton therapy facility in Israel and the entire Middle East region.
- The first clinical program is designed for 100 patients with head and neck, brain, thoracic and abdominal tumors. It runs from April 2023 to October 2024.
- This facility can be easily upgraded to 330 MeV maximum proton energy and low-intensity extraction, allowing the use of proton imaging.

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Agenda

1. Commissioning of Novel Gantry-Less Proton Therapy System
2. **Motion Management: Optical Respiratory Monitoring**

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High-speed low-noise optical respiratory monitoring for spot scanning proton therapy

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High-speed low-noise optical respiratory monitoring for spot scanning proton therapy

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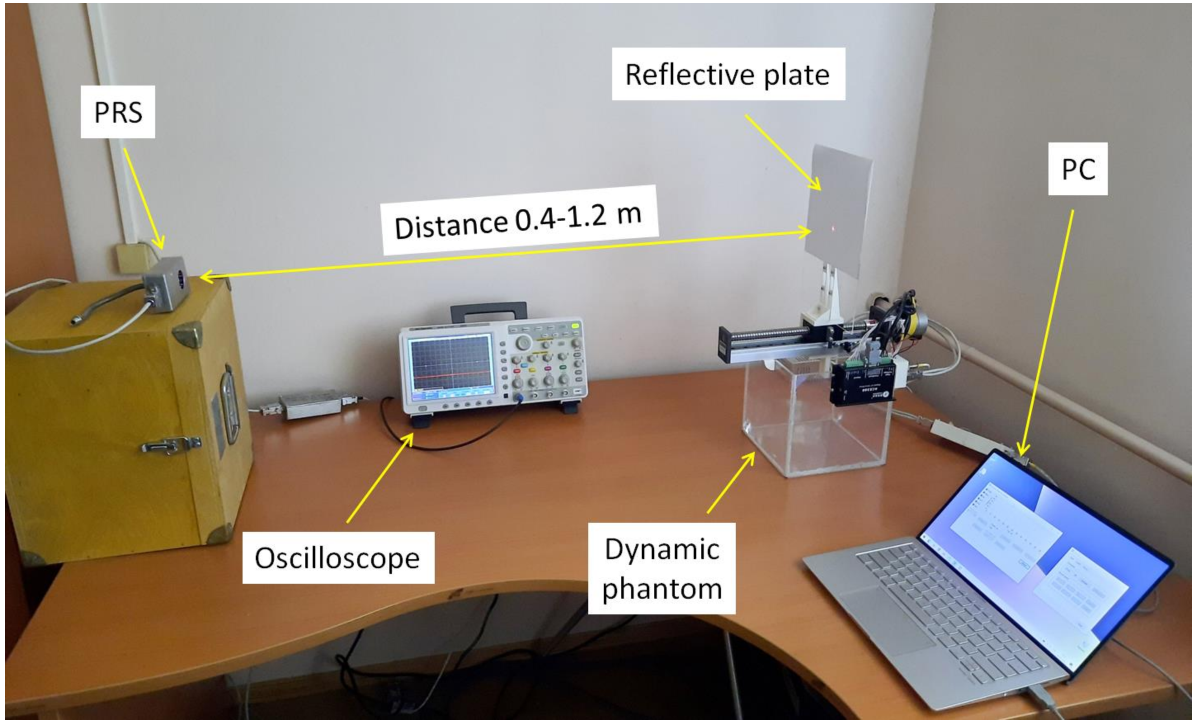
A R T I C L E I N F O

Keywords:
Spot scanning proton therapy
Respiratory monitoring
Intrafractional tumor motion
Dynamic phantom
Motion management

A B S T R A C T

Purpose: To investigate a novel optical markerless respiratory sensor for surface guided spot scanning proton therapy and to measure its main technical characteristics.
Methods: The main characteristics of the respiratory sensor including sensitivity, linearity, noise, signal-to-noise, and time delay were measured using a dynamic phantom and electrical measuring equipment on a laboratory stand. The respiratory signals of free breathing and deep-inspiration breath-hold patterns were acquired for various distances with a volunteer. A comparative analysis of this sensor with existing commercially available and experimental respiratory monitoring systems was carried out based on several criteria including principle of operation, patient contact, application to proton therapy, distance range, accuracy (noise, signal-to-noise ratio), and time delay (sampling rate).
Results: The sensor provides optical respiratory monitoring of the chest surface over a distance range of 0.4–1.2 m with the RMS noise of 0.03–0.60 mm, SNR of 40–15 dB (for motion with peak-to-peak of 10 mm), and time delay of 1.2 ± 0.2 ms.
Conclusions: The investigated optical respiratory sensor was found to be appropriate to use in surface guided spot scanning proton therapy. This sensor combined with a fast respiratory signal processing algorithm may provide accurate beam control and a fast response in patients' irregular breathing movements. A careful study of correlation between the respiratory signal and 4DCT data of tumor position will be required before clinical implementation.



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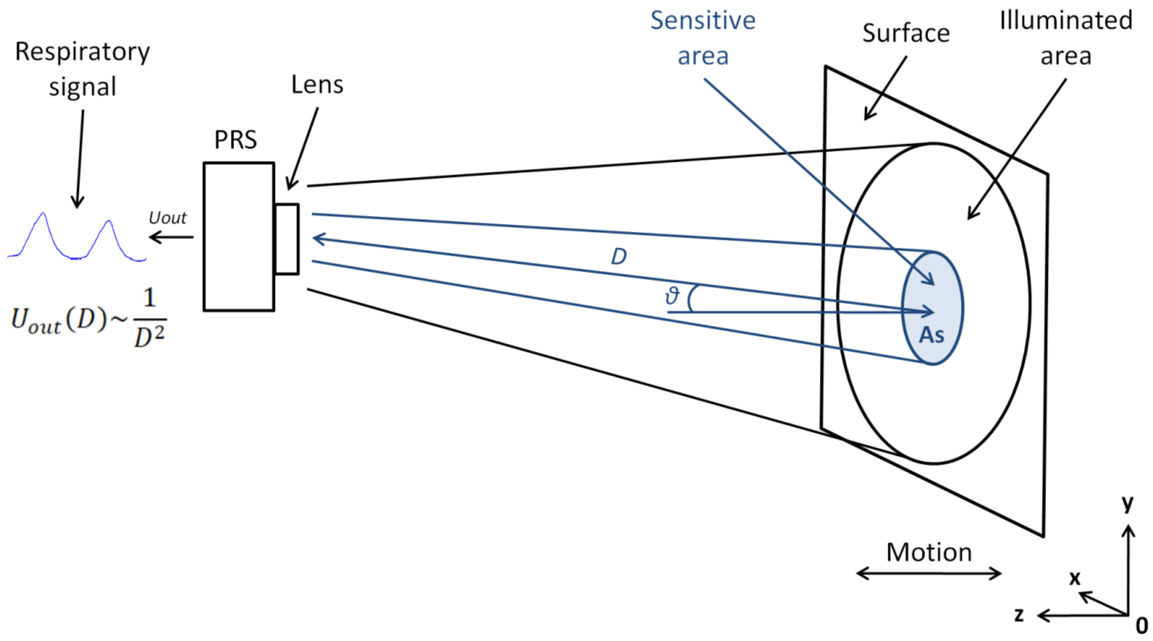
PRS: Principle of operation. Physics



- PRS (Protom respiratory sensor) monitors the motion of a moving surface and generates a signal proportional to its relative displacement.
- The LED array emits a cone shaped infrared beam (λ = 940 nm) that is reflected by the surface.
- Respiratory motion → distance change between the sensor and the surface → increase or decrease of the reflected radiation flux.
- The sensor output, which is proportional to the inverse square of the distance *D*, represents the motion signal $U_{out}(D)$ in real time.

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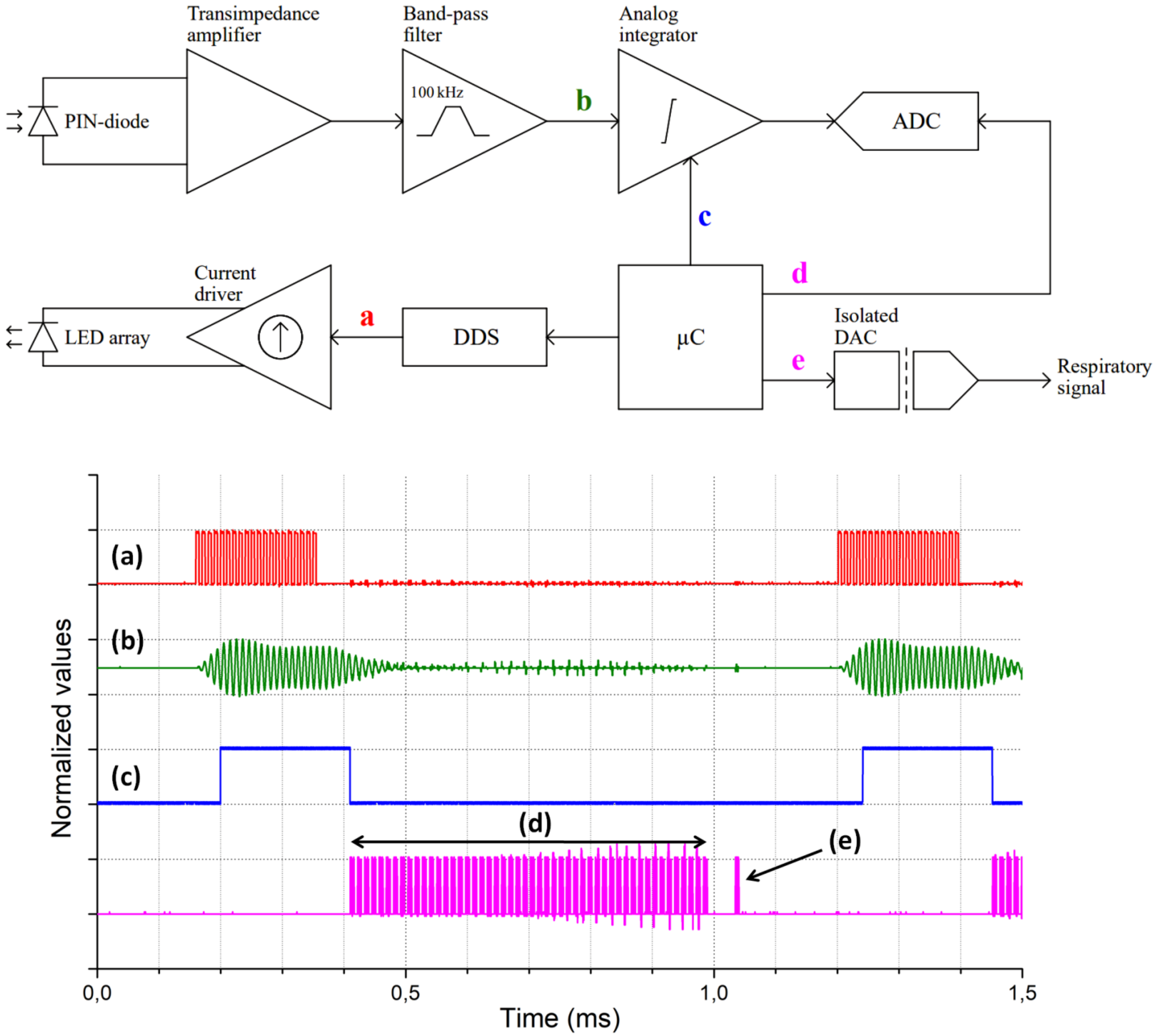
PRS: Principle of operation. Schematics

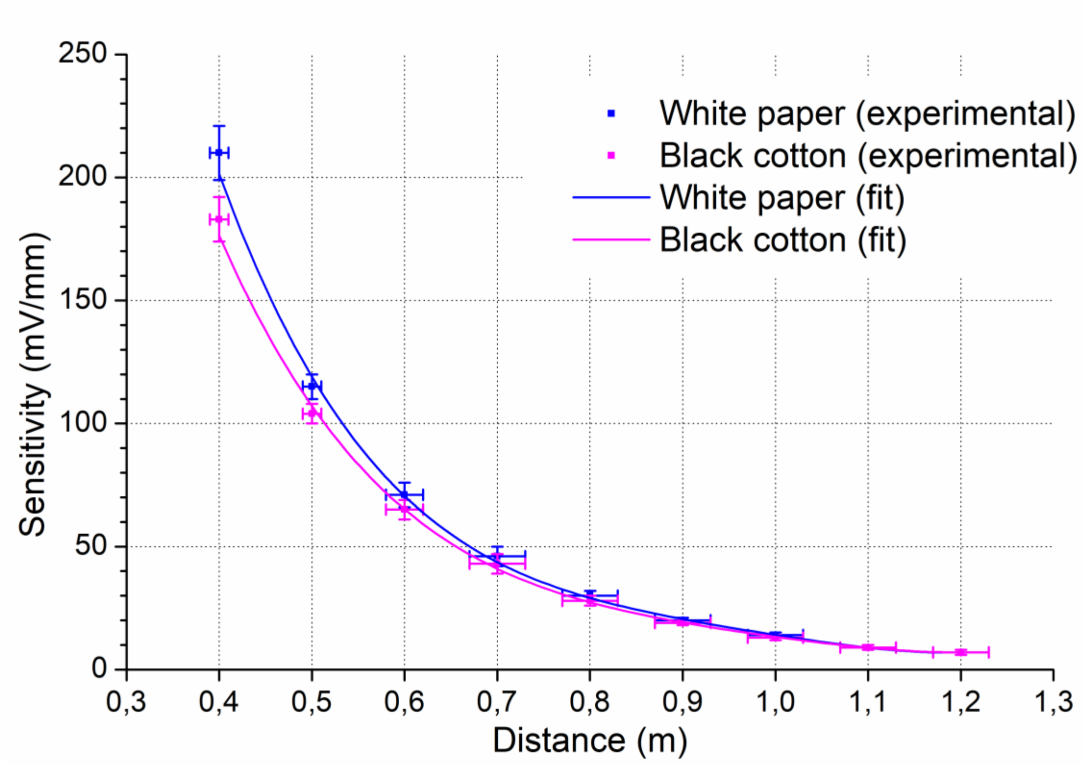


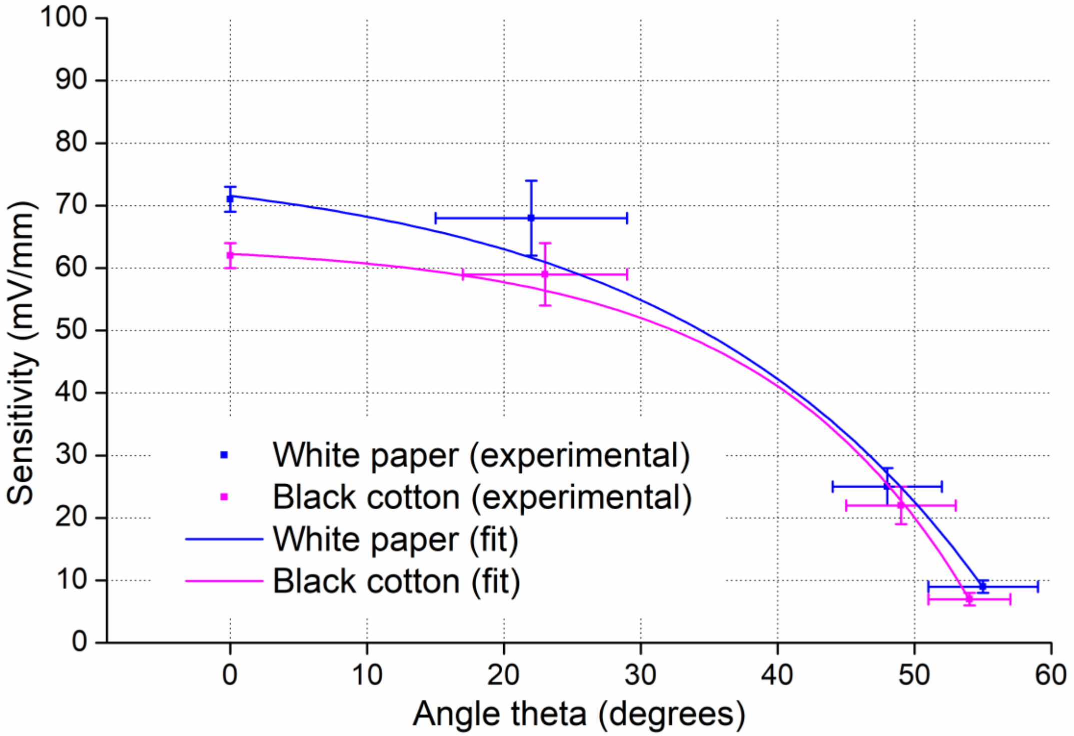
- (a) the amplitude modulated pulses for the LED array
- (b) the received reflected pulses after passing through the band-pass filter
- (c) the integrator trigger pulse,
- The clock signals (d) for the analog-to-digital converter (ADC)
- (e) for the digital-to-analog converter (DAC)

Sensitivity

$$S = \frac{\Delta U_{out}}{\Delta D}$$

The sensitivity (S, mV/mm) quantifies how the sensor responds to surface motion at a certain distance. ΔU_{out} – output signal change in mV, ΔD – surface displacement in mm.





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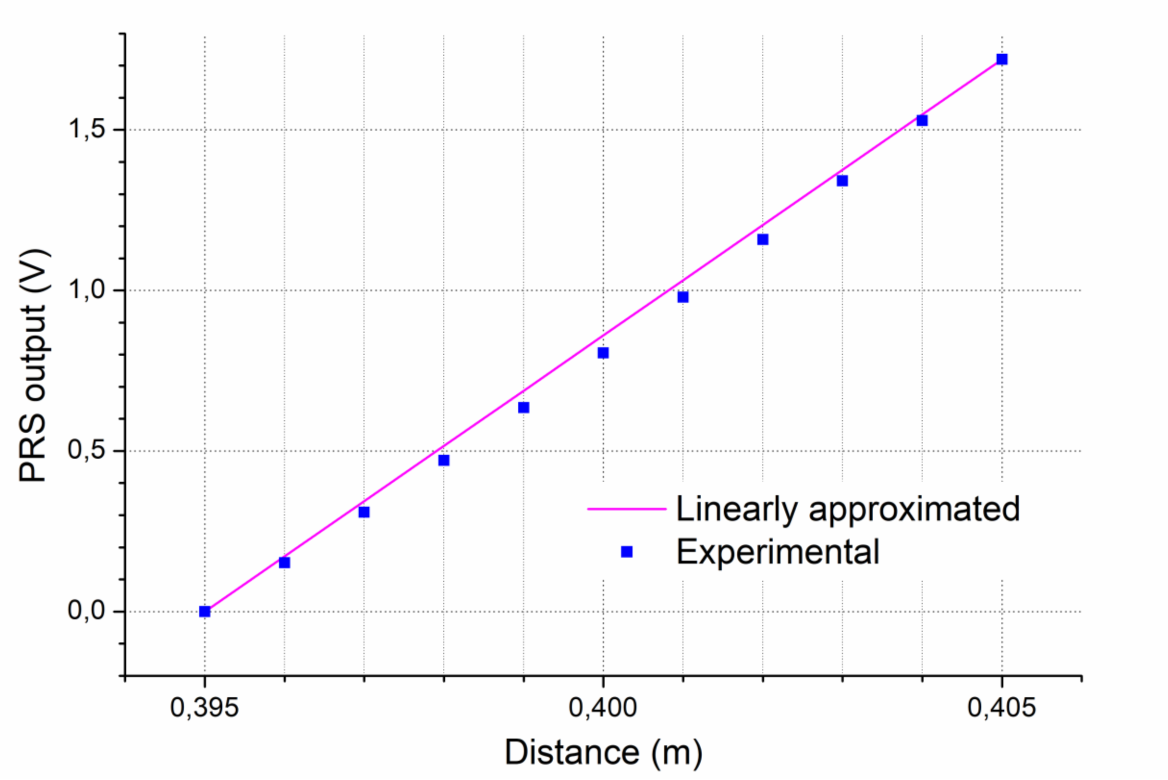
Linearity



The transfer characteristic of PRS at the nominal distance of 0.4 m

- $U_{lin}(D) = a_1 D + a_2$
- U_{lin} – output value for the linearized characteristic, a_1, a_2 – linear coefficients
- The deviation of the experimental characteristics from the modeled function was described by the absolute nonlinearity (ANL)
- $ANL = \left|\frac{U_{lin} - U_{exp}}{S(D)}\right|$
- U_{exp} – output value for the experimental characteristic

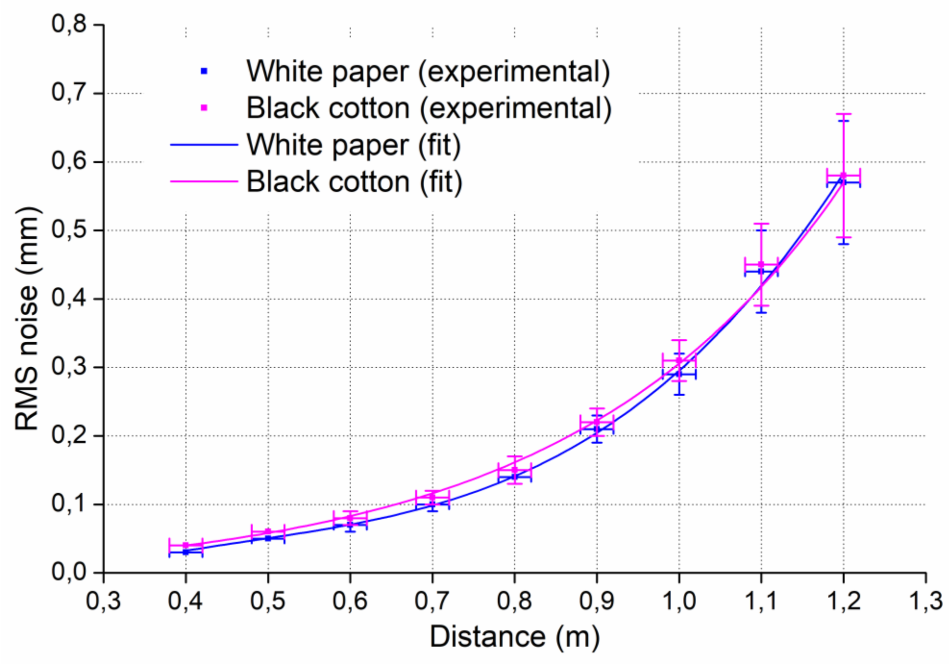
Noise

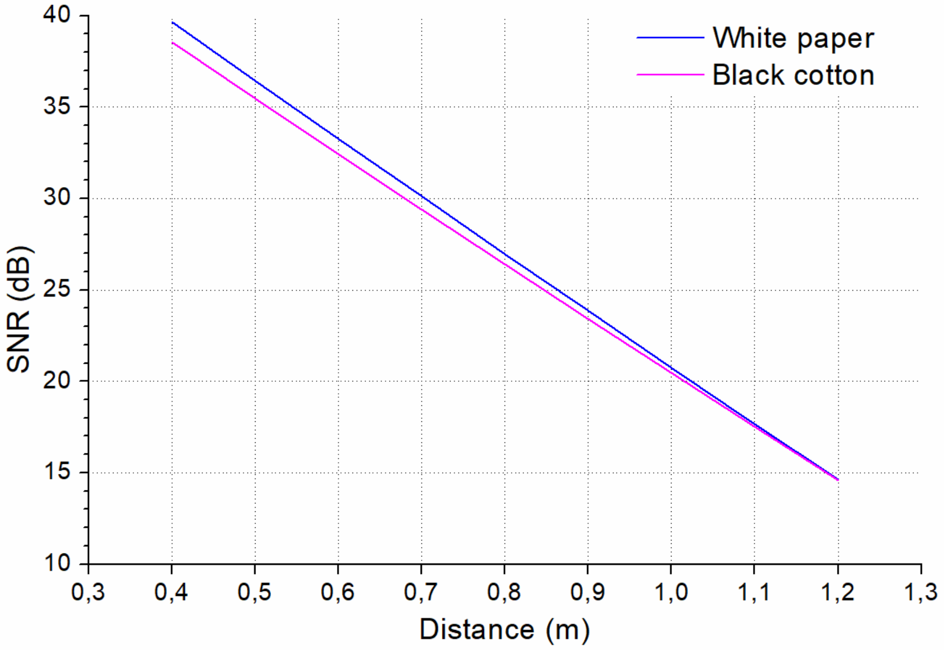
$$U_{RMS}(D) = \sqrt{\frac{\sum_{i=1}^{n}(U_i - \bar{U})^2}{n}}$$

$$SNR(D) = 20\,log_{10}\left(\frac{U_{RMS}(D)}{N_{RMS}(D)}\right)$$

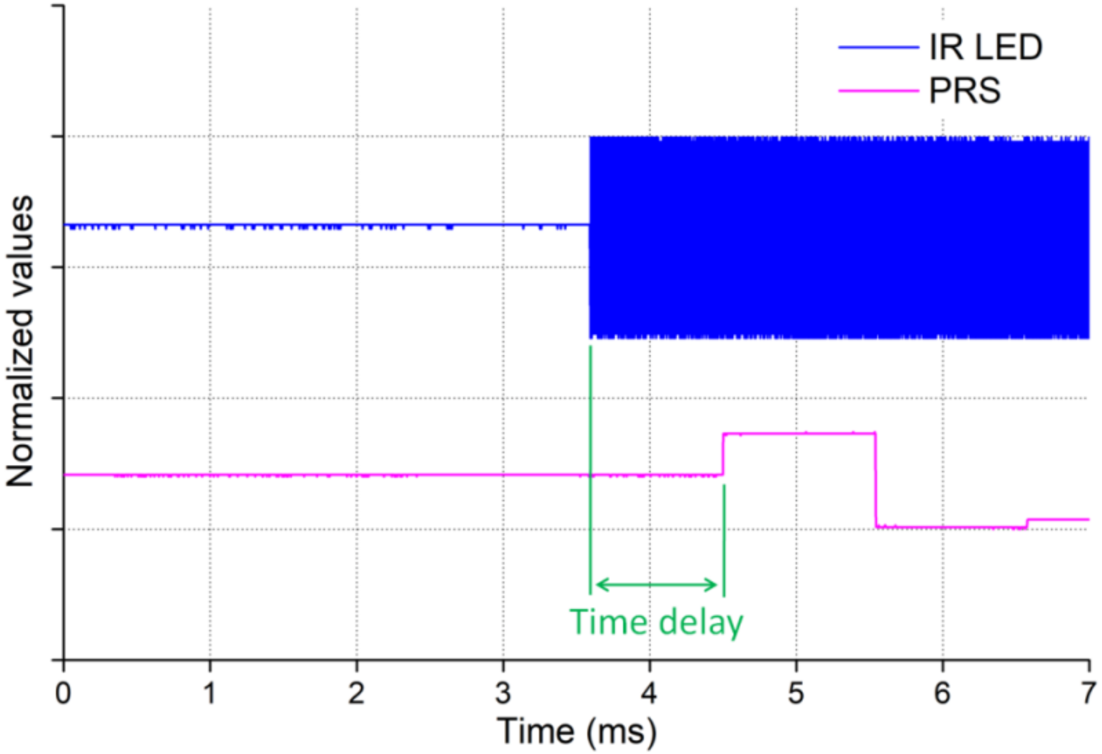
U_i – instantaneous voltage signal value, $\bar{U}$ – mean voltage signal value, n – number of instantaneous values used for the calculation of the mean

U_{RMS} – RMS value of the respiratory signal, N_{RMS} – RMS value of the noise signal



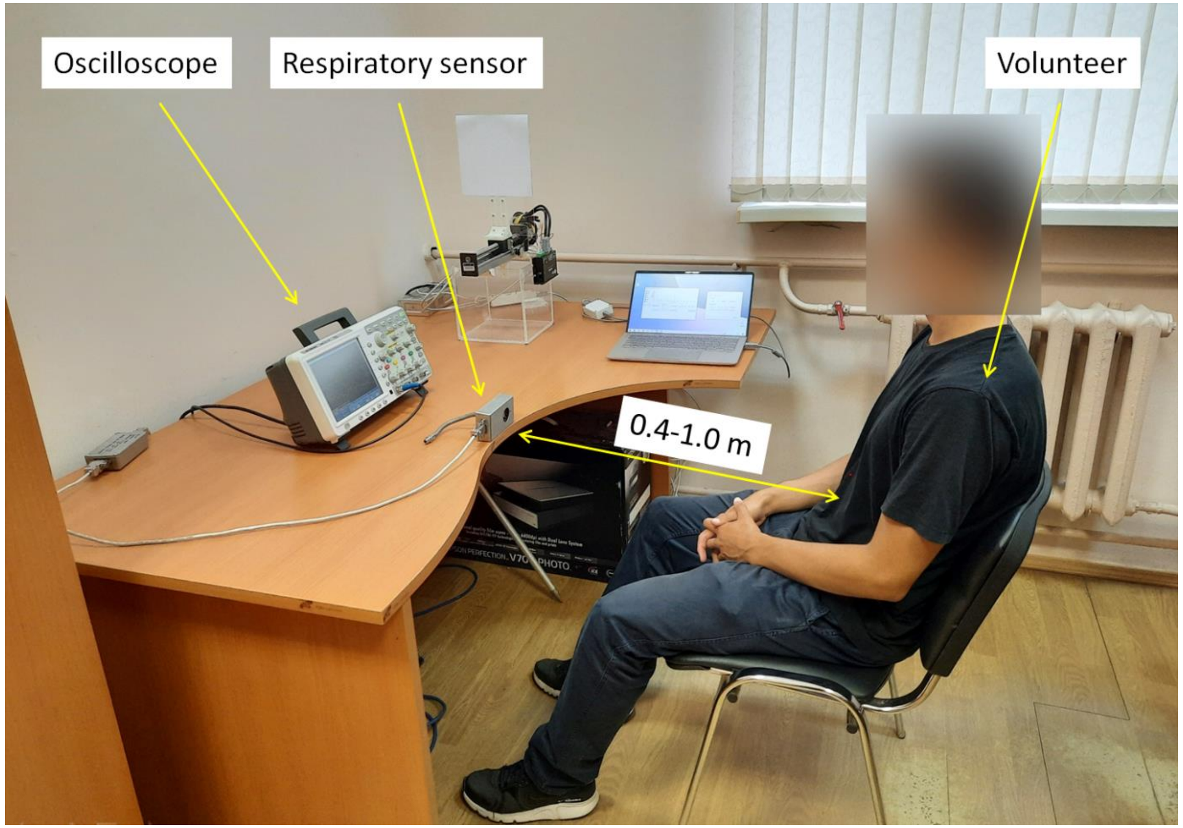


Time delay



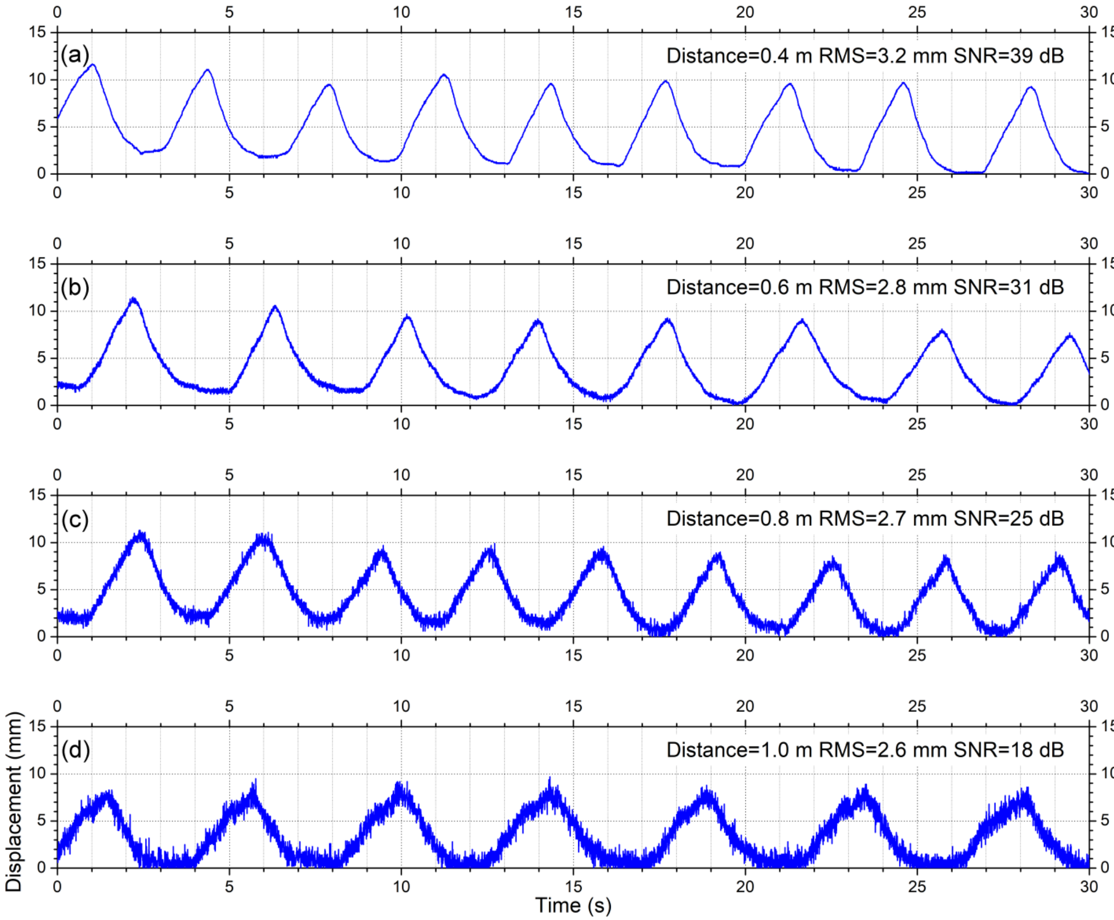
1.2 ± 0.2 ms (mean ± standard deviation).

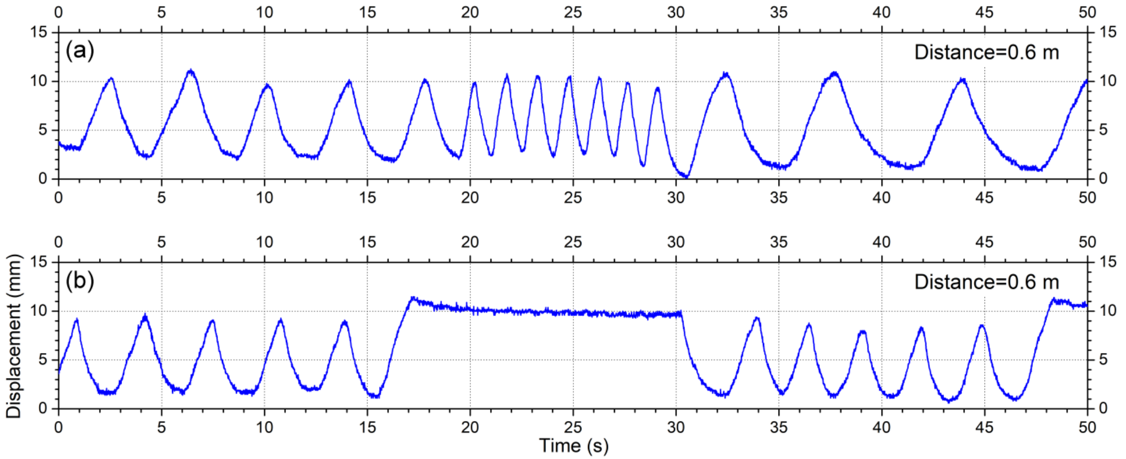
Respiratory monitoring with a volunteer



- Respiratory signals acquisition was carried out with a healthy 28-year-old volunteer dressed in a black cotton T-shirt.
- The PRS was placed on the laboratory table and the volunteer was positioned in a chair.
- The PRS was directed at the chest of a volunteer using the built-in laser pointer.
- The respiratory signals were obtained at free breathing pattern at distances of 0.4 m, 0.6 m, 0.8 m and 1.0 m, and at 0.6 m with a deep-inspiration breath-hold and a breathing pattern with intentional irregularities.

Respiratory monitoring with a volunteer





An example of the respiratory signal from a human volunteer recorded for distances of (a) 0.4 m, (b) 0.6 m, (c) 0.8 m, (d) 1.0 m. (right)

An example (a) with intentional irregularities and (b) with deep-inspiration breath-hold recorded for a distance of 0.6 m. (left)

Comparison of Surrogate Motion Monitoring Systems

System	Principle of operation	Patient contact	Application to proton therapy	Distance range	Accuracy (noise, SNR)	Time delay (sampling rate)
RPM	Tracking of marker position using CCD camera	No contact, marker	yes	NA	1.1 ± 0.9 mm	~160 ms (30 Hz)
Catalyst	Building the patient's surface map by high definition cameras and light emitters	No contact, no marker	yes	NA	< 0.5 mm (Noise < 0.1 mm, SNR ≥ 14.6 dB)	(> 15 Hz)
AlignRT	3D model of patient surface based on data from two stereo cameras	No contact, no marker	Yes	2.7 m	0.2 ± 0.1 mm (Noise < 0.5 mm)	up to 529 ms (6.5 Hz)
AZ-733VI	Belt with pressure sensor and laser distance sensor	No contact (laser) and contact (belt)	yes	< 0.25± 0.15 m (laser)	(SNR ≥ 28 dB)	3 ms (40 Hz)
Polaris SPECTRA	Detection of markers position based on photogrammetry	No contact, marker	yes	1.5 m	(Noise < 0.06 mm)	16.6 ± 1.0 ms (60 Hz)
Aurora V3	Electromagnetic field measurement	No contact, marker	yes	0.36 m	(Noise < 0.2 mm)	31.6 ± 1.0 ms (40 Hz)
Microsoft Kinect	High-resolution camera and time-of-flight sensor	No contact, no marker	NA	0.5-4.5 m	(Noise < 2 mm for 1-2 m)	(30 Hz)
SDX	Spirometry	Contact	yes	NA	NA	NA
Laser-based	Laser distance measurement	No contact, no marker	NA	0.05 - 0.15 m	(SNR = 207 for 10 mm motion)	(2 kHz)
MEMS-based	Magnetic field measurement using a MEMS-sensor	Contact	NA	≈ 0.3 m	< 0.088 mm	(< 250 Hz)
CMS	Electrical capacitance measurement	No contact, no marker	NA	< 0.1 m	(SNR ≈ 11)	(200 Hz)
Bio-impedance-based	Electrical bioimpedance measurement	Contact	NA	NA	(SNR = 3.98)	33 ms
PRS	IR radiation flux measurement	No contact, no marker	NA	0.4-1.2 m	(Noise < 0.6 ± 0.1 mm SNR > 15 dB)	1.2 ± 0.2 ms (≈ 1 kHz)

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Optical Respiratory Monitoring Conclusions

- A novel optical respiratory sensor that does not require patient attached markers was investigated and found to be appropriate to use in spot scanning proton therapy.
- In future use the sensor combined with a fast respiratory signal processing algorithm may provide accurate beam control and a fast response in patients irregular breathing movements during spot scanning proton therapy.
- A careful study of correlation between the respiratory signal and 4DCT data of tumor position will be required before clinical implementation.

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Conclusions and Outlook

- The novel gantry-less proton therapy system has been commissioned and is in clinical use.
- Developed new high-speed low-noise optical respiratory monitoring sensor technology suitable for spot scanning proton therapy

Thank you for your attention!

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