Electronic Supplementary Information for:

Laser-induced breakdown spectroscopy for cancer diagnosis and intraoperative feedback

Yikang Hou, Zhuoxi Li, Jie Lian*

School of Investigation, People's Public Security University of China, Beijing 100038, China

*Corresponding author: rlianjie@163.com

This Electronic Supplementary Information contains the detailed reporting checklist and tabular implementation roadmap that support the revised Critical Review.

Table S1: Minimum reporting checklist for clinically oriented oncologic LIBS studies. Priority: M, must report; S, should report; R, recommended for translational or deployment-oriented studies.

Reporting domain	Priority	Minimum information to report	Why it matters clinically
Patient and pathology definition	M	Number of patients, specimens, spectra, spots, and images; tumor type and grade; adjacent tissue definition; pathology reference and blinding status	Prevents spectrum-level sample inflation and clarifies whether labels reflect clinically valid ground truth
Sample state and preparation	M	Fresh, frozen, paraffin, dried drop, substrate, drying time, storage time, thaw cycles, section thickness, cleaning shots, and surface handling	Controls matrix effects and identifies whether the experiment is pathology-suite, laboratory, or operating-room relevant
Instrument and plasma window	M	Laser wavelength, pulse duration, energy at sample, spot size or fluence, repetition rate, gate delay, gate width, atmosphere, spectrometer range, and calibration checks	Determines ablation mass, plasma temperature, line broadening, continuum background, and reproducibility
Spectral preprocessing and QC	M	Baseline correction, denoising, normalization, peak integration, internal standard, feature selection, failed-spectrum policy, and whether each step was fitted within training data only	Prevents information leakage and allows another laboratory to reproduce the decision pipeline
Validation design	M	Patient-grouped split, batch holdout, external center or temporal validation, model locking, class balance, confidence intervals, and patient- or region-level confusion matrices	Distinguishes proof-of-concept performance from clinically relevant generalization
Class imbalance and augmentation	S	Pre-specified balancing method, whether augmentation was applied after patient grouping, class-specific sensitivity/specificity, and treatment of rare classes	Avoids spectrum-level or synthetic-sample leakage that can be especially severe in biofluid LIBS
Model interpretation	S	Wavelength-level importance, permutation importance, SHAP-type attribution, or equivalent explanation linked to chemically plausible variables	Helps determine whether the classifier uses disease biology rather than substrate, batch, or patient identity
Clinical endpoint and use case	M	Tissue attribution, margin distance, triage, subtype, stage, treatment response, or closed-loop stopping; latency and tolerated false-negative rate	Aligns the analytical claim with the decision that a pathologist or surgeon must make
Deployment and safety	R	Sterile interface, operator workflow, fail-safe state, low-confidence output, maintenance schedule, drift monitoring, and software update control	Converts laboratory performance into a usable clinical device or decision-support system

Table S2: Detailed clinical-implementation roadmap for oncologic LIBS. Thresholds are illustrative decision gates that should be adjusted to the clinical task and risk tolerance rather than treated as universal regulatory criteria.

Stage	Main objective	Minimum evidence or protocol	Practical deployment constraints	Example decision gate to move forward
Analytical lockdown	Stabilize the measurement before clinical claims	Fixed sample protocol; laser and gate settings; spectral acceptance criteria; calibration or internal-standard checks; pre-specified preprocessing	Hydration, blood, surface curvature, sterile covers, substrate lots, instrument warm-up, and operator-to-operator variation	Key-line or index repeatability within the pre-specified tolerance, e.g., between-day RSD $\leq$15–20% for QC material and >95% spectra passing quality criteria
Retrospective clinical validation	Test whether collected specimens contain clinically meaningful signal	Patient-grouped train/test split; pathology labels; class-specific sensitivity/specificity; confidence intervals; failed spectra counted	Archived tissue or biofluids may not match the intended fresh or intraoperative state; metadata may be incomplete	Locked model maintains clinically relevant performance, e.g., patient-level AUC $\geq$0.85 or sensitivity/specificity no worse than the predefined clinical baseline
External or temporal validation	Evaluate generalizability beyond the development set	New patients, batch, operator, instrument, or center; model locked before testing; comparison with clinical-reference baselines	Batch effects, substrate changes, instrument drift, and acquisition-order effects must be explicitly tested	Performance decrement remains within a predefined margin and confidence intervals exclude clinically unacceptable false-negative rates
Workflow simulation	Determine whether timing and output format fit the clinical task	End-to-end measurement timing; user interface; confidence thresholds; remeasurement rules; compatibility with sectioning or surgical field	Turnaround time, sterile handling, OR footprint, smoke or plume extraction, irrigation, and staff responsibilities	Result reaches surgeon or pathologist before the decision point, e.g., median pulse-to-decision latency <1 s for point feedback or total triage time <frozen-section delay
Prospective utility study	Determine whether LIBS changes decisions or outcomes	Prospective observational or interventional protocol; predefined primary endpoint; safety and false-negative monitoring; operator override	Human-factors risk, clinical liability, fail-safe design, data recording, and ethics approval	Demonstrated improvement in margin orientation, triage efficiency, or diagnostic confidence without exceeding the pre-specified false-negative or adverse-workflow threshold
Regulated multicenter adoption and surveillance	Maintain performance after adoption	Quality-management system; software version control; periodic recalibration; drift monitoring; audit of false positives/negatives; retraining governance	FDA/EU/NMPA pathway, CE or local approval, maintenance, cybersecurity, reimbursement, and cost-effectiveness evidence	Multicenter prospective performance and health-economic case support the intended use; post-deployment monitoring detects drift and triggers controlled updates