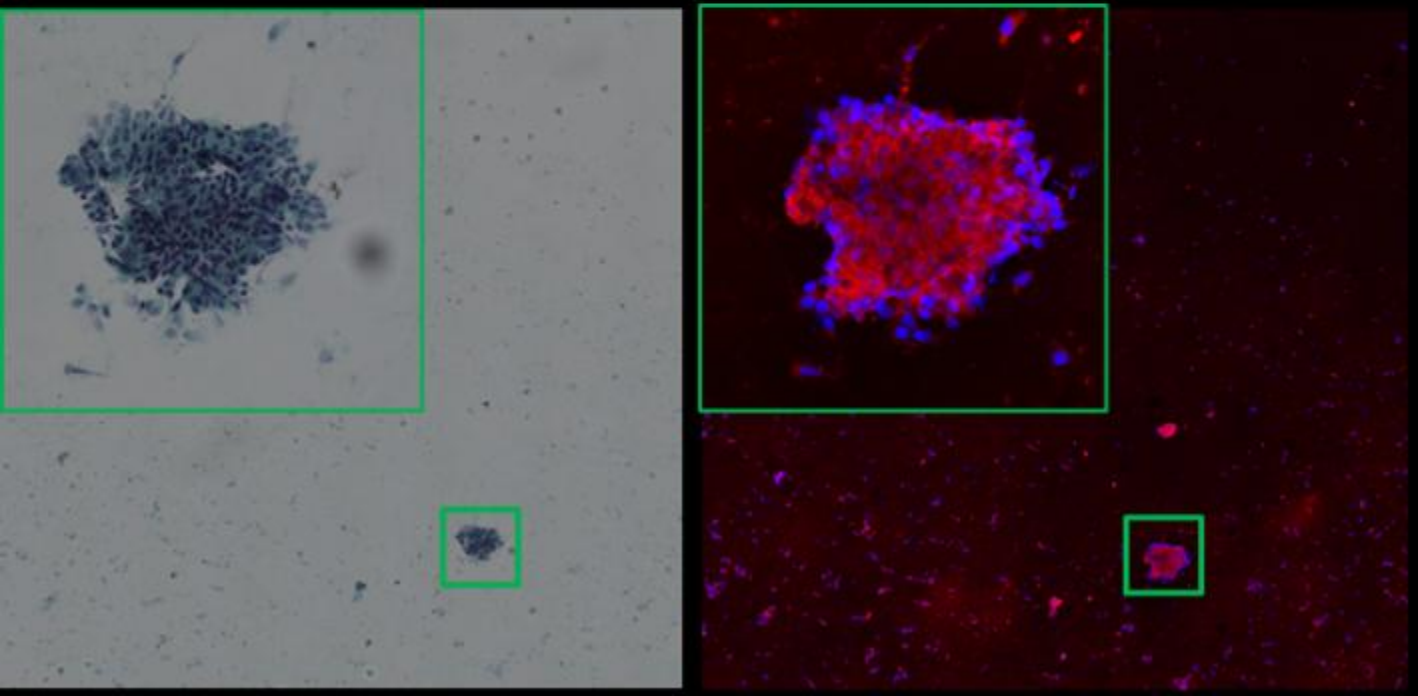
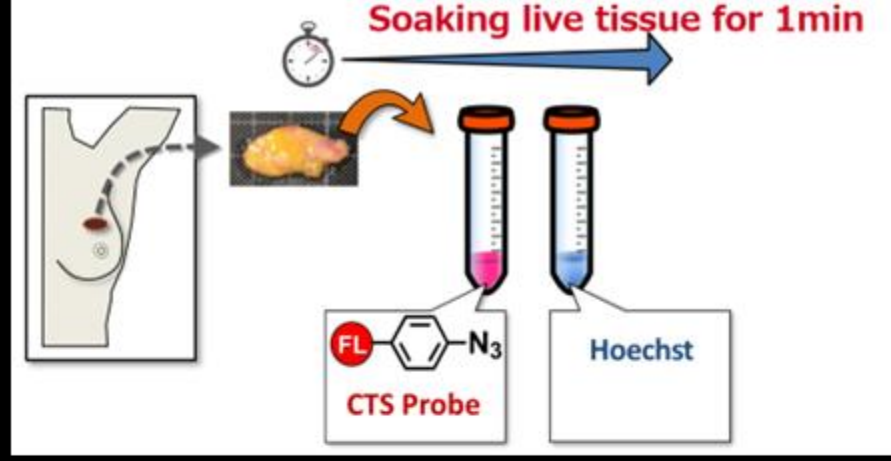
体外診断薬

CLICK-TO-SENSE法による がん術中迅速診断





B-144,144B

Establishment of a Novel Rapid and Accurate Intraoperative Assessment Method for Surgical Margin Status in Breast-Conserving Surgery and Rapid Diagnosis of Cervical Lesions Using Live-Cell Staining with the “Click-to-Sense” Assay.

「Click-to-Sense」アッセイを用いた、生細胞染色による乳房温存手術における切除断端の迅速かつ高精度な術中評価法の確立、および子宮頸部病変の迅速診断の開発

Osaka University Graduate School of Medical

Department of Breast and Endocrine Surgery
Tomonori Tanei, M.D., Ph.D., Associete Professor

国立大学法人大阪大学　大学院 医学系研究科 乳腺内分泌外科

准教授・多根井智紀

Executive Summary (1)

■ Research Objective

•To establish the **Click-to-Sense (CTS) assay** as a rapid, accurate, and objective cancer diagnostic platform.
•To transform intraoperative and outpatient diagnostic workflows.
•To standardize diagnosis through AI integration and digital pathology.
•To address the global shortage of pathologists and reduce diagnostic burden.

■ Research & Development Stage (Current Status)

•Pilot study completed in breast cancer surgery：Demonstrated diagnostic accuracy comparable to frozen section for intraoperative margin assessment.
•Ongoing application to **cervical cytology (outpatient rapid diagnosis)**.
•Integration with AI-based image analysis in progress.
•Preparing for expanded clinical trials and future regulatory strategy (PMDA).

■ Mechanism of Action / Modality

•Live-cell staining–based diagnostic assay
•Detection of cancer-associated intracellular reactions via fluorescence signaling.
•Cytology-based rapid diagnostic modality.
•Platform integration with AI-driven image analysis for objective digital diagnostics.

Executive Summary (2)

■ Target Indications

•**Breast cancer:** Intraoperative margin assessment in breast-conserving surgery.
•**Cervical lesions:** Rapid diagnostic testing in the outpatient setting.
•Future expansion to other solid tumors and cytology-based malignancies.

■ Competitive Advantages Over Existing Methods

(Compared with frozen section and conventional cytology)

Efficacy

•Comparable diagnostic accuracy to frozen section in pilot study.

Convenience

•Potential reduction of intraoperative waiting time through in-OR implementation.
•Enables rapid diagnostic testing in outpatient clinics.

Objectivity

•AI-assisted interpretation improves reproducibility and reduces interobserver variability.

Cost-effectiveness

•Reduces workload for pathologists and pathology departments.
•Potential reduction in re-operation rates and overall healthcare costs.
•Lower dependency on specialized cryosection infrastructure.

■ Desired Industry Collaboration

•Co-development of intraoperative diagnostic devices.
•Joint development of AI-based diagnostic algorithms.
•Support for clinical trials and regulatory strategy.
•Manufacturing and global commercialization partnerships.
•Expansion toward companion diagnostics and new indications.

B-144,144B

Intraoperative margin examination in breast conserving surgery for current breast caner

Backgrounds

Require more time !

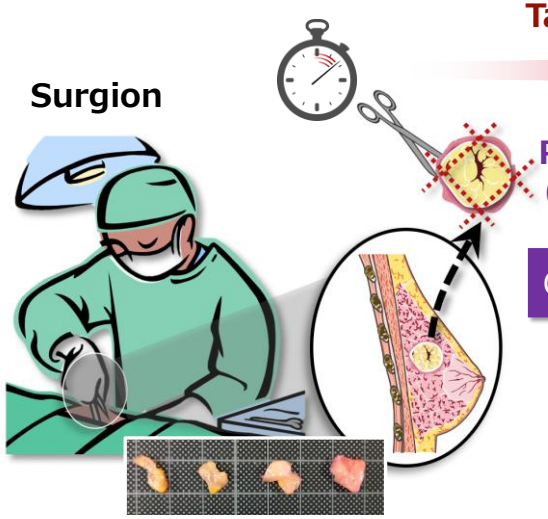
Taking about 30-40 mins

Pathologist shortage !

Surgion

Frozen tissue
Pathological diagnosis
(HE staining method)

Pathologist



Cancer Diagnosis

Re-excision

Not only the presence cancer
Identifies the form (type)

- Normal gland
- DCIS
- Invasive cancer
- Micro-cancer
- Lobular cancer
- Proliferative lesion
- Benign tumor

Targeted Goal

Objective

This study aimed to provide a quich and easy intraoperative diagnosis, staining of live tissues is performed to ditect cancer cells

▶ Previous studies of cancer diagnosis by live tissues

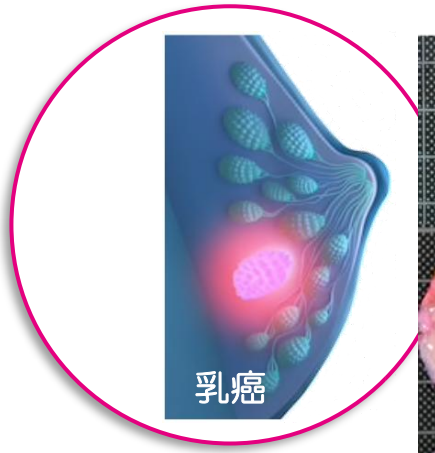
1) MarginProbe® device
(detection of cancer by radio-waves)
2) Micro CT、Micro MRI、Ex-vivo MRI
3) Antibody detection、fluorescent probes
(enzymes expressed in cancer)

- False positive rate= about 50%
- Difficult to detect micro cancer lesions.
- There are no antibody or enzymes for all cancers.
- Fluorescent probe dose not stay on cancer（unclear image）.

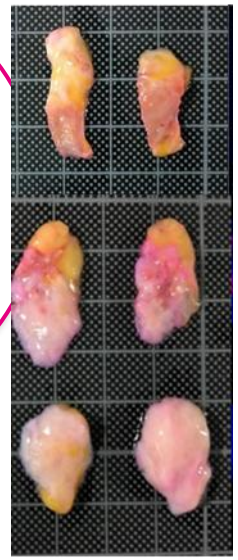
Those can not identified cancer morphology at the cellular level.

Specific visualization of cancer cells（CTS assay）

Key Data (1)



検査部位



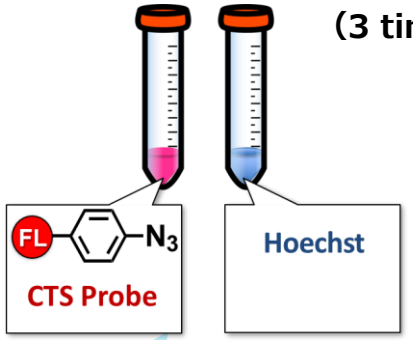
簡易術中がん診断

Click to SENSE

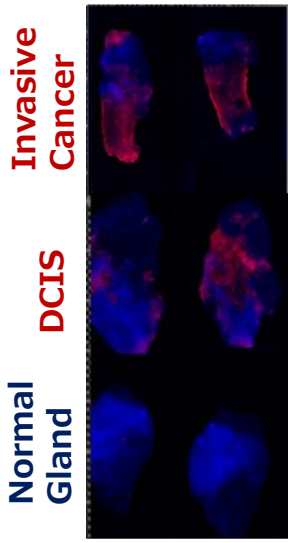
Double staining

Soaking live tissue for 5min

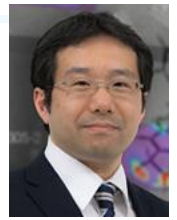
Wash by PBS (3 times)



Light up Cancer cells



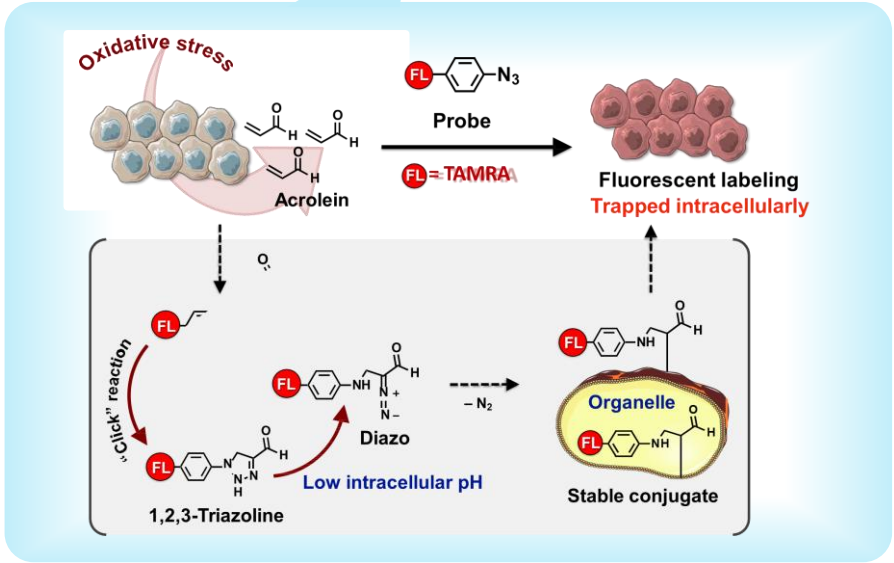
Keyence fluorescence microscope BZ-X710



Riken Katsunori Tanaka

Riken Koji Morimoto

Red : Cancer staining
Blue : Nuclear staining



Identifies the type (form) of cancer

Institute of Science Tokyo Ambara.R. Pradipta

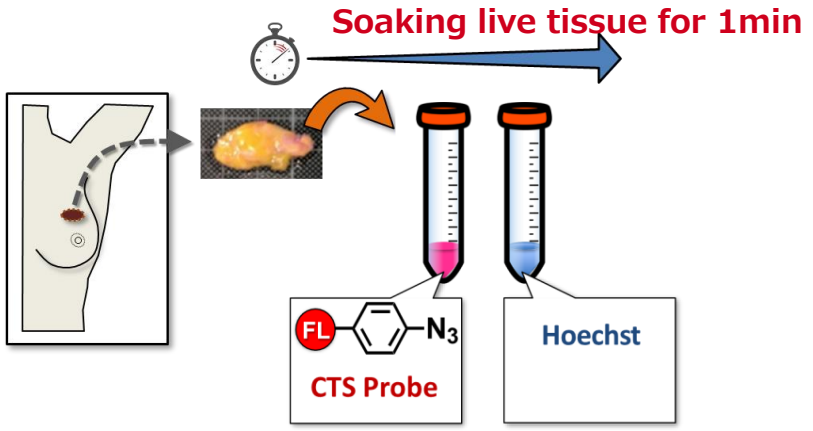
理化学研究所 RIKEN

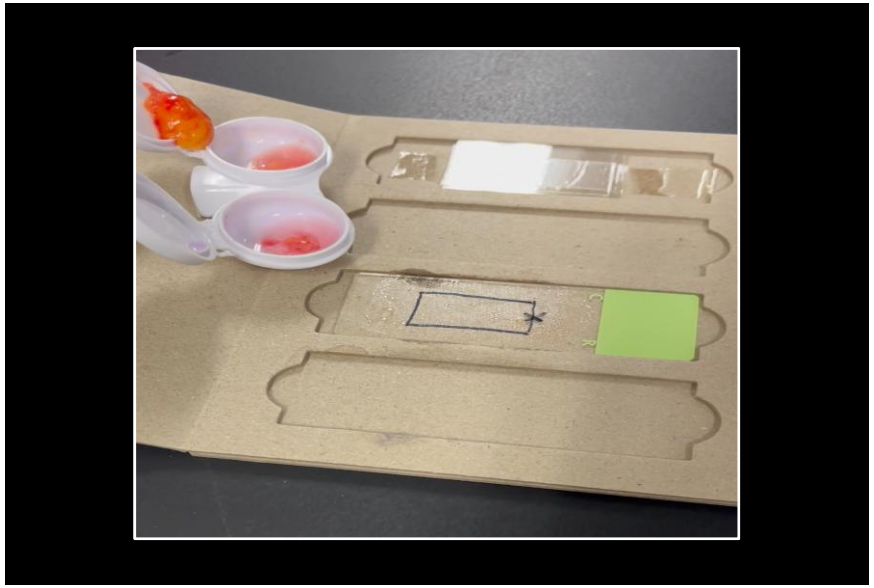
大阪大学 OSAKA UNIVERSITY

Specific visualization of cancer cells（CTS assay）

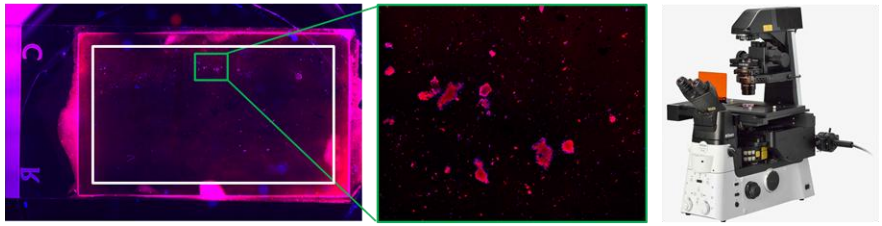
Key Data (2)

Imprint cytology using the CTS method





Immediately after staining, the slide is stamped.



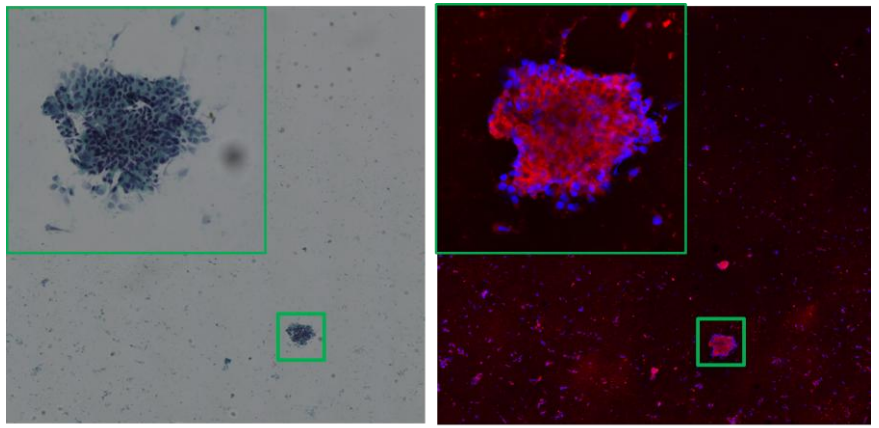
Fluorescent imaging of imprinted cells on the slide.

Nikon Eclipse Ti2

Remove the cover glass

Comparison

Papanicolaou staining of the same slide



Papanicolaou stain Positive

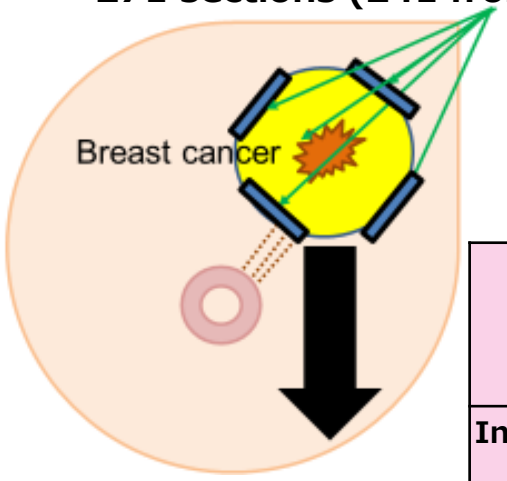
CTS method Positive

➡ Cytology is easy to focus of photo and to put into practical use.

Key Data (3)

Multicenter prospective clinical trial of CTS assay
Pilot study (March 2022 - Dec 2023)

60 cases (breast-conserving surgeries)
271 sections (241 from resection margins, 30 from central specimens)



		Postoperative permanent pathology: Positive	Postoperative permanent pathology: Negative	Overall concordance rate
CTS assay	Positive	**28**	4	**97%**
	Negative	5	**234**	
Intraoperative pathology (Frozen section)	Positive	**32**	4	**98%**
	Negative	1	**234**	

	Imprint cytology of CTS assay	Intraoperative pathology (Frozen section)
Overall concordance rate:	**97%**	**98%**
Positive concordance rate:	88%	89%
Negative concordance rate:	98%	99%
Sensitivity:	85%	97%
Specificity:	98%	98%

KBCSG-TR
Kinki Breast Cancer Study Group
Translational Research

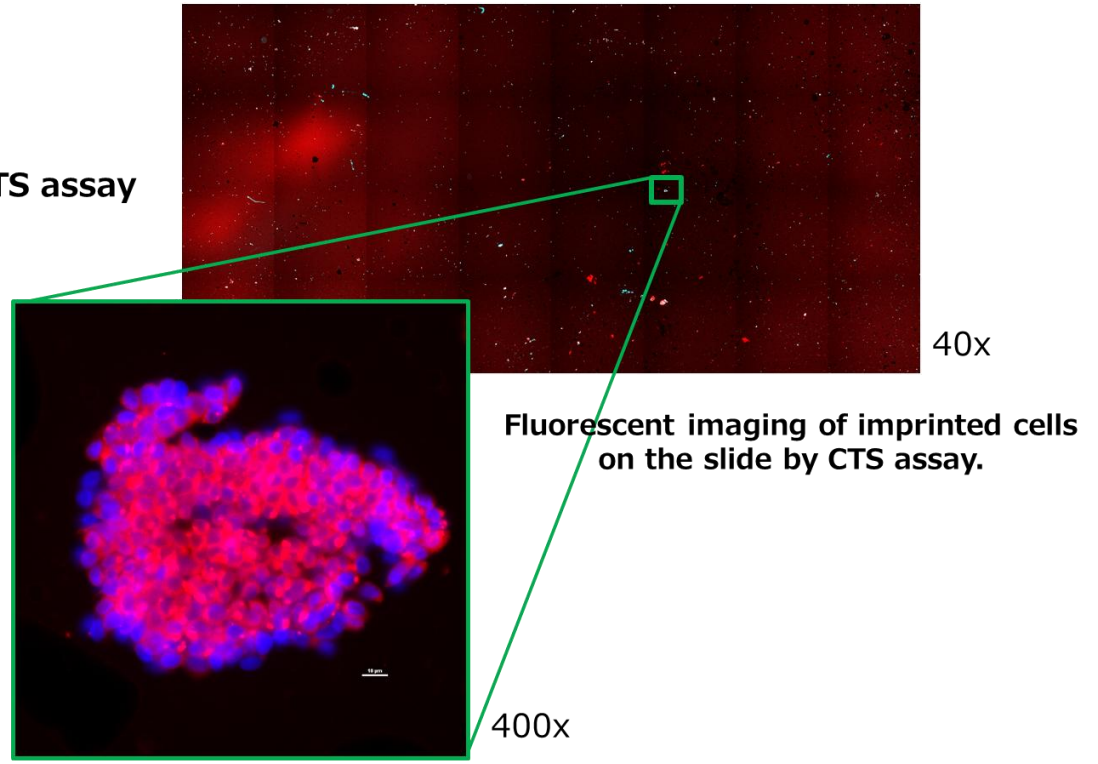
Total Glant
54,230,000yen
JSPS KAKENHI (JP22K08709, JP24K11762, and JP24K01625),
AMED (JP22ck0106783), AMED FORCE

理化学研究所
東京科学大学
大阪大学 OSAKA UNIVERSITY
AMED

Key Data (4)

A case with positive margin
CTS:＋/Frozen:＋/Permanent pathology:＋ （DCIS）

CTS assay

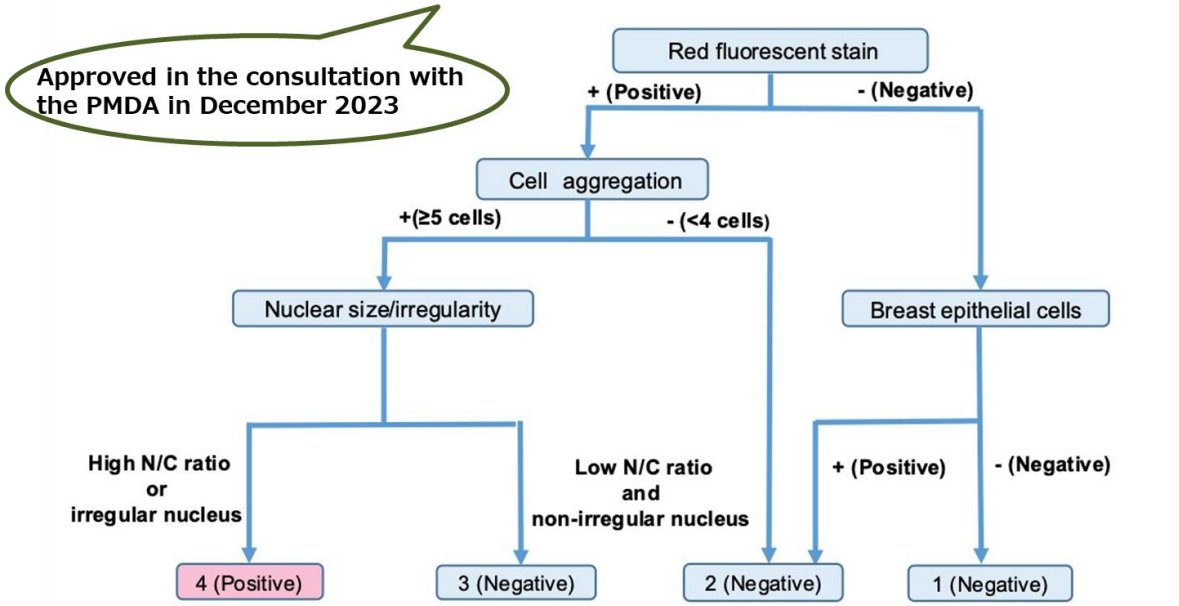


40x

400x

Fluorescent imaging of imprinted cells on the slide by CTS assay.

Flow chart showing the diagnostic criteria for the CTS assay (Visual inspection)



Attachment of the precautions

For **nuclear staining of cells (blue)**, the following criteria are excluded from positive of CTS assay.

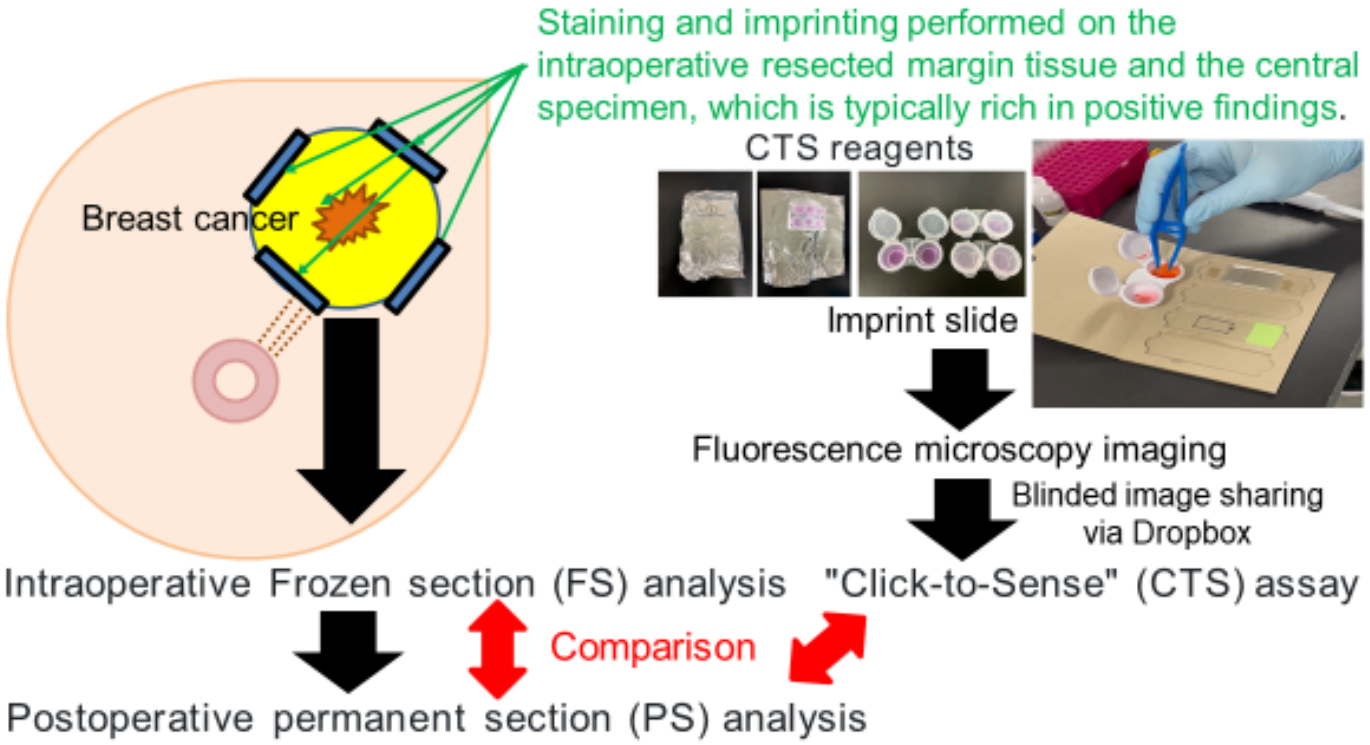
①**Small nucleus size （less than 10μm）**

②**Cells without irregular nucleus shape**

Key Data (5)

Multicenter prospective clinical trial approved by PMDA of Japan (CTS probes manufactured by company) (March 2024 -)

100 cases : breast-conserving surgeries
(Ancillary study :30 cases after Neoadjuvant chemotherapy)
Breast-conserving surgery for primary breast cancer
(Tis–T2, N0–1, M0, Stage 0–IIB)



Primary Endpoint: Overall concordance rate, positive concordance rate, and negative concordance rate between the CTS method and permanent pathological diagnosis.
Secondary Endpoint: Evaluation of the non-inferiority of the CTS method compared to intraoperative pathological diagnosis using frozen sections.

KBCSG-TR
Kinki Breast Cancer Study Group
Translational Research

Total Glant
54,230,000yen
JSPS KAKENHI (JP22K08709, JP24K11762, and JP24K01625),
AMED (JP22ck0106783), AMED FORCE

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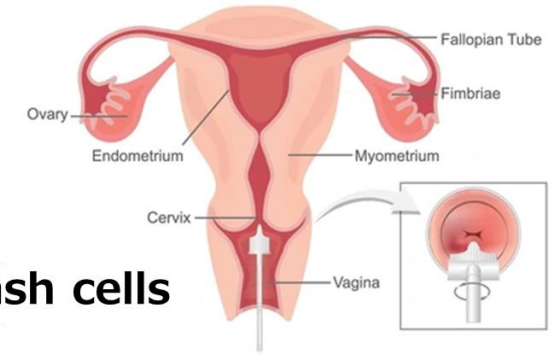
AMED

CTS assay potential for rapid outpatient testing of other cancer

Key Data (6)

CTS study of Cervical cytology

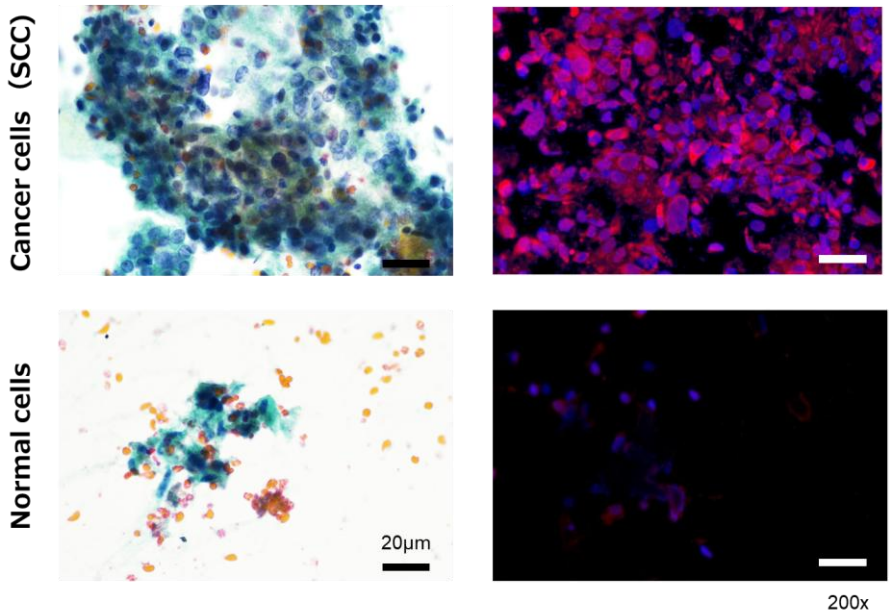


Scraping brash cells

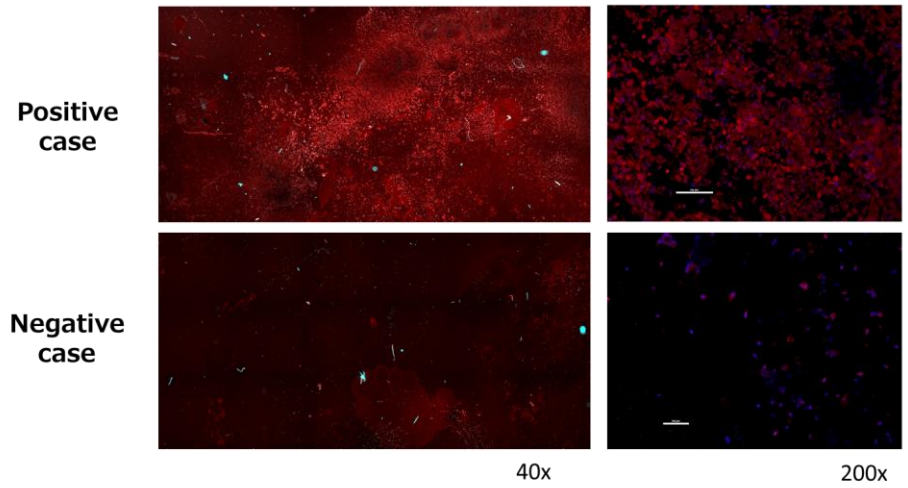
Pap Smear (Pap Test)

➡Application of CTS assay to cervical cancer screening
(collaborated with the dept of gynecology of Osaka university)

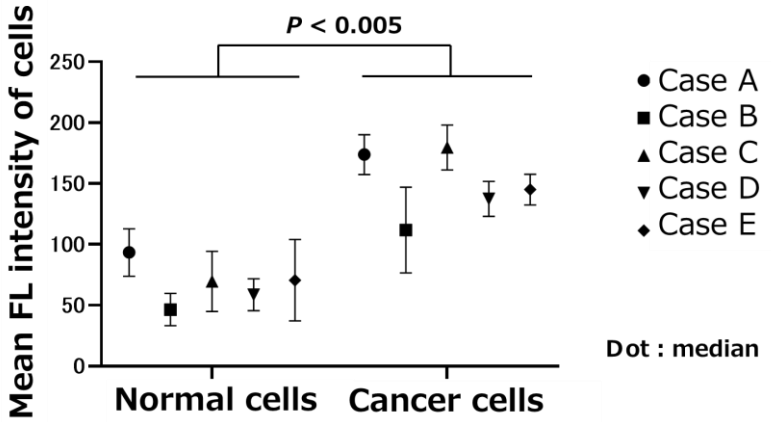
Cervical cytology



Cytological CTS assay of Cervical cancer



Fluorescence Intensity of Cervical Cells by CTS Probe



Samples collected from five patients who underwent cervical conization

Total Glant
45,000,000yen
AMED (JP25ck0106069)

CTS assay potential for rapid testing of other cancers

Key Data (7)

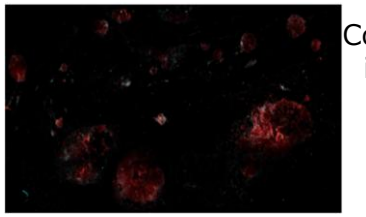
Medical examination	Diseases
Intraoperative diagnosis	**Breast cancer** margin assesment
	Colorectal cancer margin assesment
	Lung cancer margin assesment
	Bladder cancer margin assesment
	Gastric cancer margin assesment
Health check	**Cervical cancer** (cytodiagnosis)
Outpatient care	**Cervical cancer** (cytodiagnosis)
	Breast cancer (Fine-needle aspiration)
	Lung cancer (Bronchial brushing cytology)
	Oral cancer (oral cytology)

We aim to extend the application of CTS assay to a variety of other cancers.

Key Data (8)

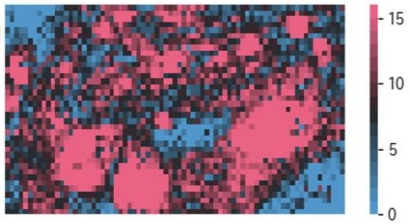
CTS imaging analyzed by AI in collaboration with Information science and techonology of Osaka university (Dr. S.Seno)

The image of CTS assay

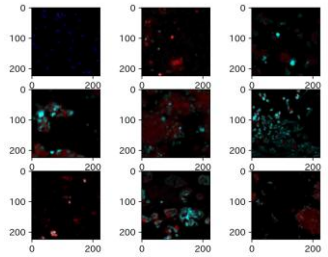


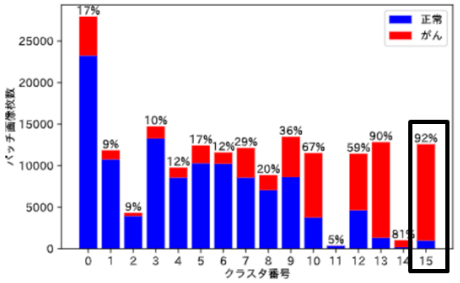
Color cording in clusters

Cancer characteristic domein



Patches of clustering





Cancer:92%

Seed	Training			Validation			Testing	fraction	
0	0.915	0.877	0.001	0.905	0.873	0.001	0.891	**0.870**	**0.003**
1	0.868			0.833			0.922		
2	0.849			0.881			0.797		

91 breast cancer images, 118 normal gland images
Shuffled with training: validation: testing=5:2:3

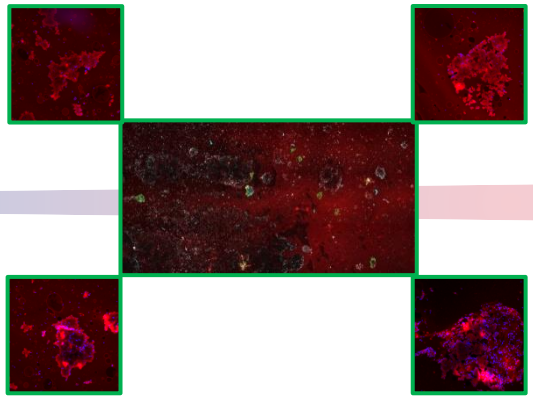
➡ **AI could discriminate cancer or normal images with 87%.**

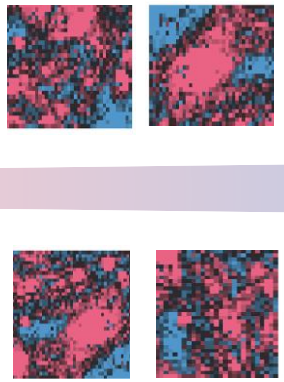
To make the CTS assay practical use, develop a medical device microscope includes AI

Microscopic programing software

Imaging analyzed by AI

Nikon Eclipse Ti2
Fluorescent microscope





Diagnosis (Detection)

➡ **We would like to join with microscopic company.**

Competitive Advantage

The CTS assay represents a next-generation rapid diagnostic platform of **high level accuracy, AI-driven objectivity, and operating-room, rapid outpatient testing–integrated workflow optimization.**

Innovation

- **Rapid diagnostic technology using live-cell staining (CTS assay)**
  A novel intraoperative diagnostic concept that can potentially replace conventional analysis.
- **Pilot study demonstrates diagnostic accuracy comparable to frozen section of breast surgery**
- **AI-integrated design**
  Integration with AI-based image analysis enables improved objectivity and reproducibility.
- **Designed for future in-operating-room or rapid outpatient testing of device implementation**
  Potential to fundamentally transform surgical or outpatients testing workflow.

Competitive Advantage

The CTS assay represents a next-generation rapid diagnostic platform of **high level accuracy, AI-driven objectivity, and operating-room, rapid outpatient testing–integrated workflow optimization.**

■ Efficacy

- Comparable diagnostic accuracy to frozen section in pilot study.
- Expected further improvement and standardization through AI integration.

■ Convenience

- Potential reduction of intraoperative waiting time through in-OR implementation.
- Simplified workflow without extensive specimen transport and cryosection preparation.

■ Safety

- Minimizes tissue loss by utilizing live-cell evaluation.
- Reduced interobserver variability and human error via AI-assisted diagnosis.

■ Cost-effectiveness

- Reduction of workload for pathologists and pathology departments.
- Potential decrease in re-operation rates, leading to overall healthcare cost reduction.
- Lower dependency on highly specialized infrastructure.

Competitive Advantage

The CTS assay represents a next-generation rapid diagnostic platform of **high level accuracy, AI-driven objectivity, and operating-room, rapid outpatient testing–integrated workflow optimization.**

Strategic Value for Industry

- Provides a solution to the global shortage of pathologists.
- Establishes a scalable platform combining surgical support devices and AI diagnostics.
- Expandable beyond breast cancer to other malignancies (e.g., cervical lesions).
- Strong potential for global market deployment.

Goal and its Plan for Research and Development

To establish the **Click-to-Sense (CTS) assay** as a globally deployable, AI-integrated rapid diagnostic platform that:

- Replaces or complements frozen section in intraoperative margin assessment
- Enables rapid outpatient cytology-based cancer diagnosis
- Standardizes diagnostic quality independent of institutional resources
- Reduces surgical waiting time, re-operation rates, and pathology workload

Challenges to achieving the goal

1. Clinical Validation

•Conduct large-scale prospective multicenter trials in breast cancer surgery
•Clinical validation in cervical lesions (outpatient setting)
•Exploration of additional solid tumor applications

2. AI Integration and Digital Platform Development

•Development of robust AI-based image analysis algorithms. Reduction of interobserver variability
•Creation of automated scoring and decision-support systems. Construction of a scalable cloud-based or device-embedded platform

3. Device Development and OR Implementation

•Development of compact intraoperative diagnostic device. Optimization of workflow for operating-room use
•Reduction of total diagnostic turnaround time. User-interface design for surgeons and clinical staff

4. Regulatory and Quality Strategy

•Early consultation with PMDA (Japan). Definition of regulatory pathway (medical device vs IVD)
•GMP-compliant manufacturing system establishment
•Preparation for global regulatory submissions (FDA/CE in future phase)

5. Strategic Industry Collaboration

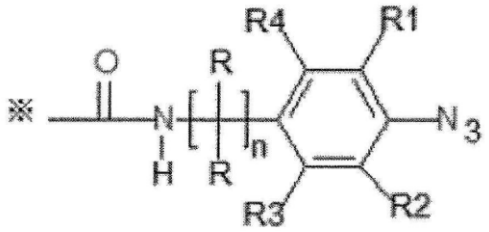
・Medical device manufacturers (hardware integration), and AI/diagnostic software companies
・Clinical trial and regulatory support partners, and Global commercialization partners

Time Schedule; Roadmap for Clinical Implementation of the CTS Assay in Breast Cancer and Cervical Cytology

Phase	Period	Subtitle	Main Development Activities	Milestone
Phase 1	2026–2027	Analysis of multicenter clinical trials on surgical margins in breast cancer; Analytical validation of cervical cell specimens; Protocol optimization; Pilot study	• Analysis of multicenter clinical trials of the CTS method for margin assessment in breast cancer surgery and AI-based image analysis	Establishment of fundamental performance data; Development of infrastructure for initiation of clinical research
			• Optimization of procedures and conditions for the CTS method using cervical scrape cytology specimens; establishment of interpretation criteria	
			• Single-center pilot study of the CTS method for cervical scrape cytology; comparison with Pap staining cytology and histopathological diagnosis	
			• Pre-consultation with PMDA	
Phase 2	2027–2029	Prospective clinical trial of cervical cell specimens and data analysis	• Conduct and analysis of a single-center PMDA clinical trial (evaluation of diagnostic performance: Accuracy, PPV, NPV)	Initial proof of clinical utility; Finalization of clinical trial design
			• Construction of AI-based image analysis platform	
			• Establishment of GMP-compliant manufacturing system	
Phase 3	2030–	Regulatory approval and social implementation	• Health economic evaluation	Establishment of clinical evidence; Practical implementation in clinical settings; Initiation of international expansion
			• Validation of AI-integrated diagnostic system; PMDA submission and regulatory approval	
			• Commercialization as an IVD product	
			• Implementation in breast surgery and gynecology departments	
			• Preparation for international expansion	

Reference（Patents / Key Papers）

Patent: **“Reagent for Reaction with Acrolein, Its Use, and Novel Compounds”**



Registered in the following five countries:

JP Patent No. 7157438 Registered: October 12, 2022 Term expires: July 6, 2038
US US12122918 Registered: October 22, 2024 Term expires: October 28, 2041
DE DE 3831888 Registered: September 6, 2023 Term expires: July 5, 2039
GB GB 3831888 Registered: September 6, 2023 Term expires: July 5, 2039
FR FR 3831888 Registered: September 6, 2023 Term expires: July 5, 2039

A reagent for reaction with acrolein comprising a compound having the chemical structure represented by Formula.
Further claims include structure-defined reagents, compounds, reaction methods, and methods for detecting acrolein.
Patent Holder: National Research and Development Agency RIKEN (Patent Holder No. 503359821)

●Tanei T, Pradipta AR, Morimoto K, Morii E, Noguchi S, Tanaka K. Cascade Reaction in Human Live Tissue Allows Clinically Applicable Diagnosis of Breast Cancer Morphology. Adv Sci (Weinh).2018 Nov 27;6(2):1801479.
●Pradipta AR, Fujii M, Tanei T, Morimoto K, Shimazu K, Noguchi S, Tanaka K. Tetramethylrhodamine is an essential scaffold of azide probe in detecting cellular acrolein. Bioorg Med Chem. 2019 Jun 1;27(11):2228-2234.
●Pradipta AR, Tanei T, Morimoto K, Shimazu K, Noguchi S, Tanaka K. Emerging Technologies for Real-Time Intraoperative Margin Assessment in Future Breast-Conserving Surgery. Adv Sci(Weinh).2020 Mar17;7(9):1901519. (A.R.P. and T.T. contributed equally to this work）
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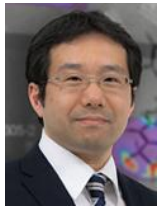
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Proposed Partnership Scheme; Development and Commercialization of the CTS (Click-to-SENSE) Platform

The CTS (Click-to-SENSE) method aims to be practically implemented in:Rapid intraoperative margin assessment in breast cancer surgery, or cervical cytology diagnostics with the ultimate objective of obtaining regulatory approval and achieving international expansion as an AI-integrated in vitro diagnostic (IVD) medical device.

In this research project, academia will take the lead in establishing robust clinical evidence.
Through close collaboration with industry partners, we aim to achieve the following:

- Kit development and commercialization of CTS probes
- Development of an AI-integrated medical device microscope
- Kit development and commercialization of CTS probes
- Establishment of a GMP-compliant manufacturing system
- Obtaining regulatory approval from PMDA
- Commercialization and global market expansion