Indocyanine green fluorescence imaging system as an alternative to the conventional sentinel lymph node mapping using a radiotracer in breast cancer

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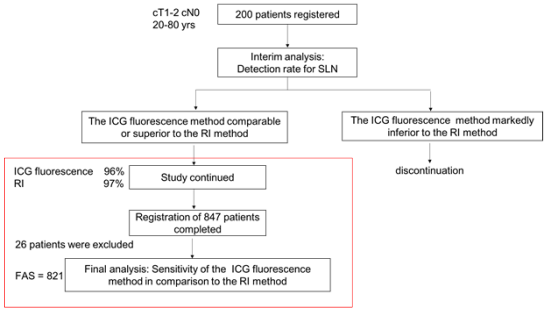
Endopoint

PRIMARY: Sensitivity of sentinel lymph node (SLN) biopsy for indocyanin green (ICG) fluorescence compared to radioactivity in the patients with tumor-positive nodes.

SECONDARY: Comparison of the detection rate for SLN, and adverse events and reactions related to ICG administration.

This trial is registered with UMIN000005167

Schema of Study



The scheduled interim analysis for the first 200 patients confirmed that detection rate of 96% for ICG fluorescence was comparable to 97% for radioactivity (Yasojima H., et.al. SABCS 2013, P1-01-03). Thereafter, a total of 847 patients were enrolled and 821 were subject to final analyses.

Methods

Patients with T1-2 primary breast cancer without lymph node metastasis were assigned in this study. A combination of ICG fluorescence and radioisotopes (RI) was applied in the patient. A real-time navigation surgery by ICG florescence imaging enabled surgeons to identify SLNs to be excised. A gamma probe was used to verify no residual radioactivity in the axilla after SLN removal. Lymph nodes removed were examined separately according to the order of removal, as the first SLN and the further nodes and classified in terms of ICG fluorescence and radioactivity.

Results

Table1 Characteristics of patients

	No	%
Age (median, range)	55	(22-80)
Menopausal Status		
Premenopausal	356	43
Postmenopausal	465	57
BMI (median, range) kg/m2	22.1	(14.9-38.8)
Pretreatment		
none	751	91
chemotherapy	70	19
Tumor size		
T1	526	64
T1a	13	
T1b	97	
T1c	376	
unclassified	40	
T2	295	36
Sentinel status		
Negative	641	78
Positive	180	22
Number of SLN removed (average, range)		
RI	1.73	(0-6)
ICG fluorescence	2.27	(0-9)

Fig.1 Concordance and discordance between RI and ICG (%; n/N)

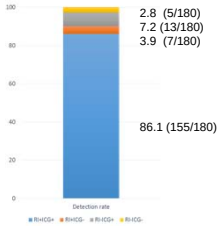


Table 2 Sensitivity for ICG fluorescence

	% (n/N; 95%CI)	p
Sensitivity compared with RI as a gold standard method	95.7 (155/162; 91.3- 98.3)	0.11*

A lower limit of 95 % CI (confidence interval) could not exceed pre-specified threshold value of 93%. This study concludes that the ICG fluorescence method is not superior but comparable to the RI method.

Table 3 Detection rate for positive SLN (N=180)

	% (n/N; 95% CI)	,p
Pts. with positive SLN	22 (180/821)	
Positive SLN detected by		
RI	90.0 (162/180; 84.7-94.0)	-
ICG fluorescence	93.3 (168/180: 88.6-96.5)	0.18
Combination of both	97.2 (175/180: 93.6-99.1)	<0.001

Fig. 2 Overall detection rate SLN (%; n/N)

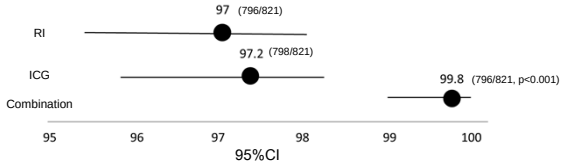


Table 4 Detection rate for SLN after chemotherapy

	% (n/N; 95% CI)	p
No chemotherapy (N=751)		
RI	97.5 (732/751; 82.3-96.8)	-
ICG fluorescence	96.9 (728/751; 95.4-98.1)	0.63
After chemotherapy (N=70)		
RI	91.4 (64/70; 82.3-96.8)	-
ICG fluorescence	100 (70/70; 94.9-100)	0.04

There is no serious adverse event related to hypersensitivity to ICG.

Summary and Conclusions

- The ICG fluorescence method achieves a high detection rate of SLN comparable to that of the RI method (97.2% vs 97.0%)
- A combination of ICG and RI yields a significant improvement of SLN detection compared with radioactivity alone (99.8% vs 97%, p<0.001)
- The detection rate for ICG fluorescence is significantly superior to radioactivity after neoadjuvant chemotherapy (100% vs 91.4%, p=0.04)
- These results of this study confirm that ICG fluorescence imaging system is an alternative and/or additive to the conventional SLN mapping using a radioactive tracer in breast cancer

References

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