



Utility of circulating tumor cell (CTC) in advanced gastric cancer

Won Suk Lee¹, Jeong Min Kim¹, Woo Sun Kwon¹, So Jung Lim¹, Tae Soo Kim^{1,3}, Ga Yun Kim⁵, Sung Ho Choi⁵, Byung Hee Jeon⁵, Jong Rak Choi⁶, Hong Jae Chon^{1,4}, Min Kyu Jung^{1,3,4}, Joong Bae Ahn^{1,2,3,4}, Hyun Cheol Chung^{1,2,3,4}, Sun Young Rha^{1,2,3,4}
¹Song-Dang Institute for Cancer Research, ²Brain Korea 21 PLUS Project for Medical Science, Yonsei University, ³Yonsei Cancer Center, ⁴Department of Internal Medicine, Yonsei University College of Medicine, ⁵CytoGen, Seoul, Republic of Korea, ⁶Department of Laboratory Medicine, Yonsei University College of Medicine

INTRODUCTION

➢ Gastric cancer (GC) is the second most common cancer worldwide. Despite developments and improvement in diagnosis and therapy, the mortal types of gastric cancer are reflect their tendency for metastasis.

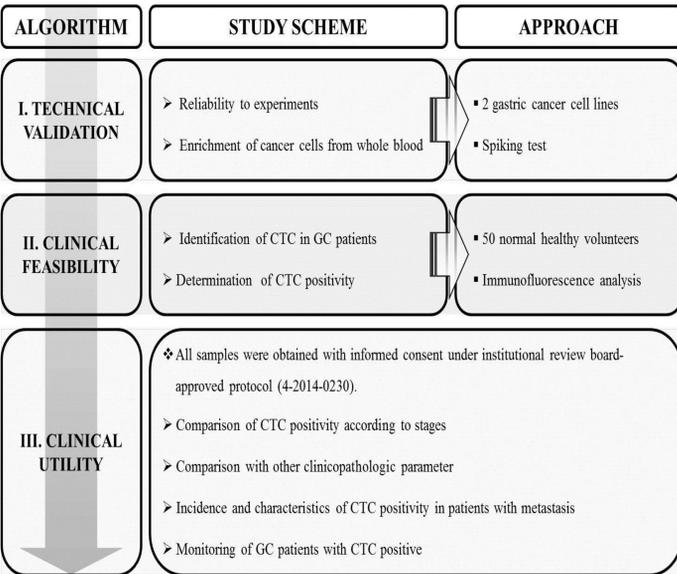
➢ The metastatic cancers are believed to derive from microscopic residual diseases in the lymph nodes, bone marrow or peripheral blood. Circulating tumor cells (CTCs), known as the “leukemic phase” of solid tumor, are detected in the peripheral blood of metastatic cancer patients.

➢ Previous reports are concerned CTCs detection technology, prognosis, drug resistance and phenotypic characterization of the cancers. However, fewer studies reported CTC isolation and their characteristic and usefulness as an indicator in GC.

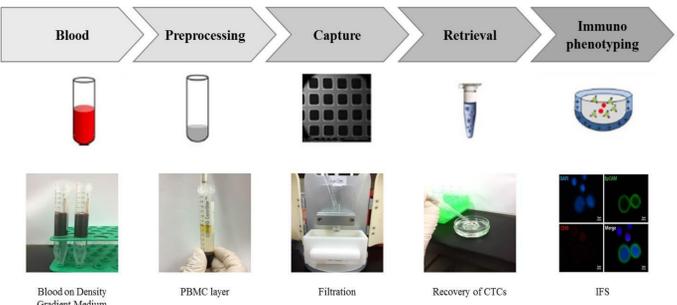
STUDY GOAL

- Detection and characterization of CTCs from human gastric cancer
- Evaluation for utility of CTC in advanced gastric cancer patients

STUDY SCHEME



MATERIALS & METHODS



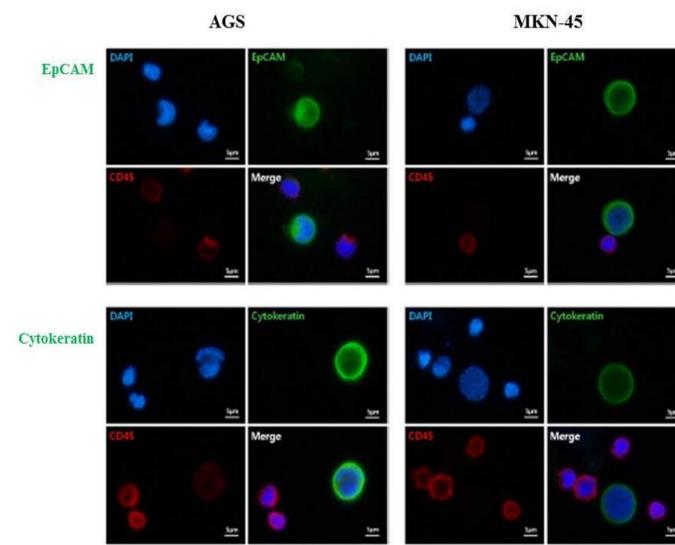
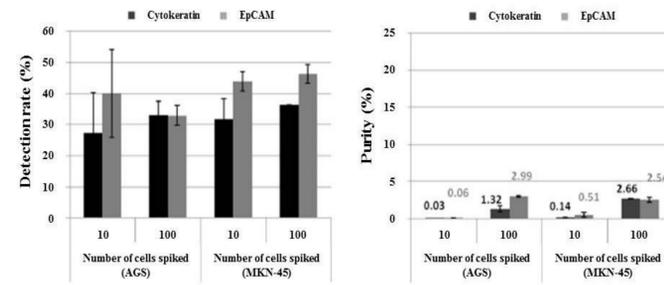
◆ Spiking test & Immunofluorescence analysis

✓ GC cell lines (AGS, MKN-45) were spiked into 5 ml of blood and were passed through the CTC platform (10 and 100 cells of AGS, MKN-45 cells/1 ml whole blood).

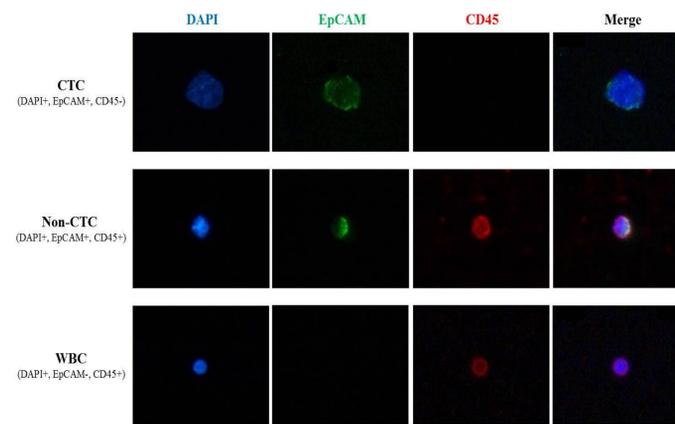
✓ Captured cells were characterized by IF staining; DAPI (nucleated cell marker; 4',6-diamidino-2-phenylindole-2HCl); cancer cells by EpCAM and WBCs by CD45.

RESULTS

Increase of reliability to experiments and enrichment of cancer cells from whole blood



Identification of circulating tumor cell in gastric cancer



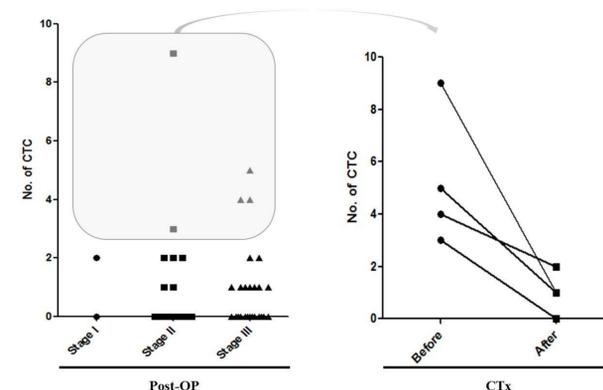
Variables	Total (n=50)	%
Age	Median (min-max)	44 (24-62)
Sex	Male	19 (38.0)
	Female	31 (62.0)
Number of CTC	0	34 (68.0)
	1	13 (26.0)
	2	3 (6.0)

Number of CTC for cut-off: 2

➔ Determination of CTC positivity through number of CTC in healthy volunteers

CTC positivity of operable gastric cancer patients (Stage I ~ III)

Variables	Total (n=66)	%	No. of CTC positive (9/66, 13.6%)	Median & range of CTC (4, 3-9)
Age	Median (min-max)	59 (30-86)		
Sex	Male	44 (66.7)		
	Female	22 (33.3)		
Stage (AJCC7)	I	14	2/14 (14.3%)	- (3-4)
	II	21	2/21 (9.5%)	- (3-9)
	III	31	5/31 (16.1%)	4 (3-5)
Cell type	AWD / AMD	20	3/20 (15.0%)	4 (3-4)
	APD / SRC	45	6/45 (13.3%)	4 (3-9)
	Mucinous	1	0/1 (0.0%)	-
Lauren classification	Intestinal	16	1/16 (6.3%)	4 (-)
	Diffuse	39	6/39 (15.4%)	4 (3-9)
	Mixed	5	0/5 (0.0%)	-
	Unknown	6	2/6 (33.3%)	- (3-4)
Operation	Pre	20	4/20 (20.0%)	3.5 (3-4)
	Post	46	5/46 (10.9%)	4 (3-9)



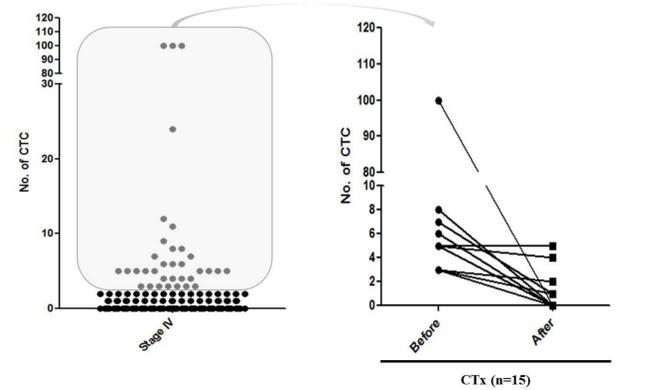
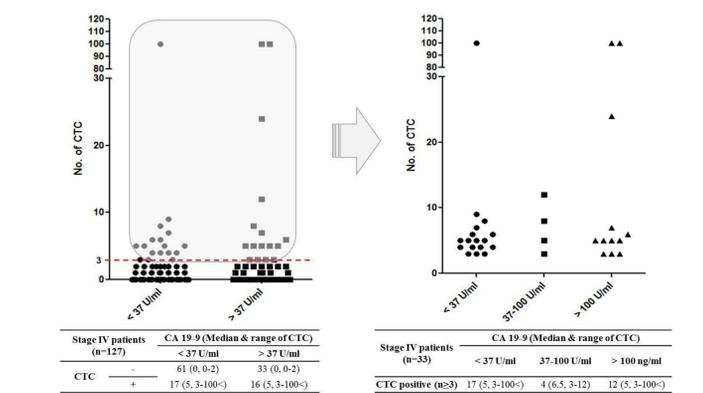
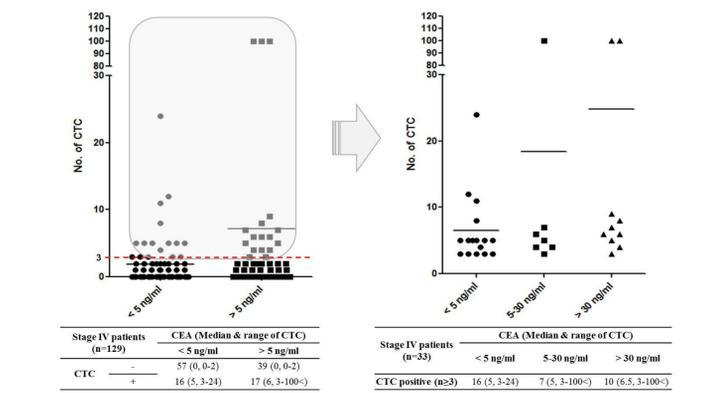
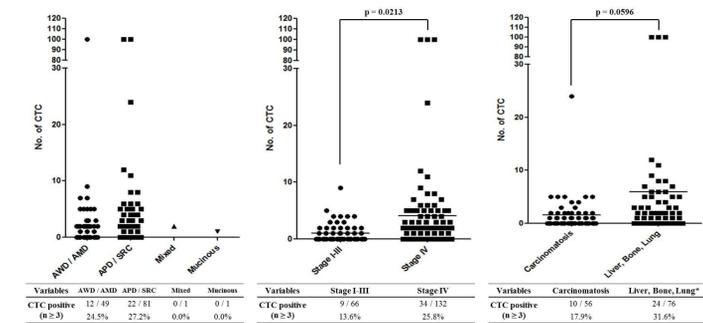
* Adjuvant chemotherapy (n=4)

RESULTS

CTC positivity of Stage IV gastric cancer patients in comparison with clinicopathologic features

Variables	Total (n=132)	%	No. of CTC positive (34/132, 25.8%)	Median & range of CTC (5, 3-100 ⁻)
Age	Median (min-max)	56.5 (31-82)		
Sex	Male	94 (71.2)		
	Female	38 (28.8)		
Cell type	AWD / AMD	49 (37.1)	12/49 (24.5%)	5 (3-100 ⁻)
	APD / SRC	81 (61.4)	22/81 (27.2%)	5 (3-100 ⁻)
	Mixed	1	0/1 (0.0%)	-
	Mucinous	1	0/1 (0.0%)	-
Lauren classification	Intestinal	16	4/16 (25.0%)	5 (3-100 ⁻)
	Diffuse	20	5/20 (25.0%)	4 (4-100 ⁻)
	Mixed	2	1/2 (50.0%)	11 (-)
	Unknown	54	24/54 (44.4%)	5 (3-100 ⁻)
HER2 expression	Positive	27	8/27 (29.6%)	7.5 (4-12)
	Negative	96	26/96 (27.1%)	5 (3-100 ⁻)
	Unknown	8	0/8 (0.0%)	-
CEA	Positive	56	17/56 (30.4%)	6 (3-100 ⁻)
	Negative	73	16/73 (21.9%)	5 (3-24)
	Unknown	3	1/3 (33.3%)	5 (-)
CA19-9	Positive	49	16/49 (32.7%)	5 (3-100 ⁻)
	Negative	78	17/78 (21.8%)	5 (3-100 ⁻)
	Unknown	5	1/5 (20.0%)	11 (-)
Metastasis	Carcinomatosis	56	10/56 (17.9%)	5 (3-24)
	Liver, Bone, Lung*	76	24/76 (31.6%)	6 (3-100 ⁻)

* Patients who have systemic metastasis (liver, bone, lung) accompany with distant lymph node and carcinomatosis.



CONCLUSION

- ❖ CTC positivity in GC is correlated with stage and systemic metastasis reflecting hematogenous metastasis.
- ❖ CTC might be a useful prognostic and monitoring indicator of gastric cancer patients.