

## Tumor stage prediction study of hepatocellular carcinoma using Alginate-graphene oxide hybrids

충남대학교병원 내과<sup>1</sup>, 대구보건대학교 임상병리학과<sup>2</sup>, 충남대학교 의과학과<sup>3</sup>, 인하대학교 생명공학과<sup>4</sup>

조현철<sup>1</sup>, 은혁수<sup>1</sup>, 이태희<sup>2</sup>, 고연오<sup>2</sup>, 이규감<sup>2</sup>, 최희권<sup>3</sup>, 김하늘<sup>3</sup>, 최정현<sup>4</sup>, 박현성<sup>4</sup>, 손채연<sup>4</sup>, 부지윤<sup>4</sup>

**Background/Aims:** It could be expected a good prognosis for patients with hepatocellular carcinoma (HCC). A plethora of candidate biomarkers using liquid biopsy, which circulating tumor cells (CTCs) are being investigated as biomarkers for the diagnosis and prognosis of different cancers, including HCC. The diagnosis method using CTC, which is a non-invasive diagnostic method has recently emerged. In this study, by adding graphene oxide to the existing our CTC isolation beads, we investigated whether it could be used in clinical practice by increasing the isolation efficiency of antibody-specific HCC cells.

**Methods:** Seven HCC male patients who received outpatient and inpatient treatment from May to December 2021 at Chungnam National University Hospital were included. Blood samples from these seven patients diagnosed with HCC were collected and clinicopathological information for these patients was investigated in detail through a retrospective review of medical records. Alginate-polyvinyl alcohol (PVA)-graphene (APG) beads were prepared in the sequence of our experiments. This research was approved by the Institutional Review Board of Chungnam National University Hospital (approval no. CNUH 2020-10-088-014).

**Results:** The APG bead methods does not require equipment such as centrifugation and microfluidic system, and it also has the advantage that it is possible to mass-produce without external pressure. Especially, added graphene oxide enable to increase the separation efficiency of antibody-specific cells by allowing more antibodies to be stably fixed to the bead. This technique allows the rapid and high concentration separation of desired cells in the blood. We analyzed the correlation between CTC count, tumor number, tumor size, HCC stage, serum AFP, and serum PIVKA-II. As shown in the figure below, the CTC counts have a significant correlation with HCC stage and serum PIVKA-II. It was confirmed that the cancer stage had the greatest correlation with the CTC count among the factors.

**Conclusions:** By using APG beads in HCC patients, it is expected that it will not only be able to non-invasively diagnose HCC early, but also can be used actively for clinical diagnosis and treatment by predicting the tumor burden.

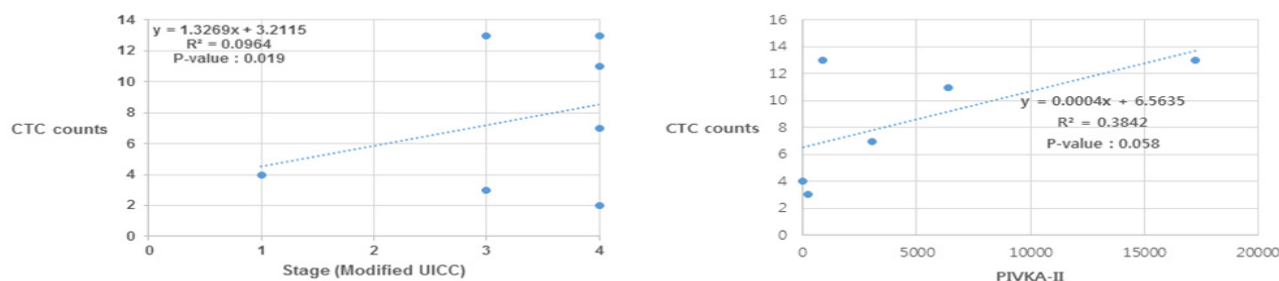


Figure 1. Correlation analysis between CTC, stage, and PIVKA-II in HCC patients

Table 1.

Baseline Characteristics of 7 Patients with hepatocellular carcinoma

Age (years)

Range (mean) 56-80 (63)

Sex

Males, n (%) 7 (100%)

Females, n (%) 0 (0%)

Child-Pugh classification

A 3 (42.8%)

B 4 (51.2%)

Etiology of cirrhosis

Hepatitis B 3 (42.8%)

Hepatitis C 1 (14.2%)

Hepatitis B & Alcohol 1 (14.2%)

Hepatitis C & Alcohol 1 (14.2%)

None 1 (14.2%)

Serum AFP level

< 20 ng/mL 3 (42.8%)

20-200 ng/mL 2 (28.5%)

> 200 ng/mL 1 (14.2%)

Missing 1 (14.2%)

Note. -HCC = hepatocellular carcinoma, AFP = alpha fetoprotein