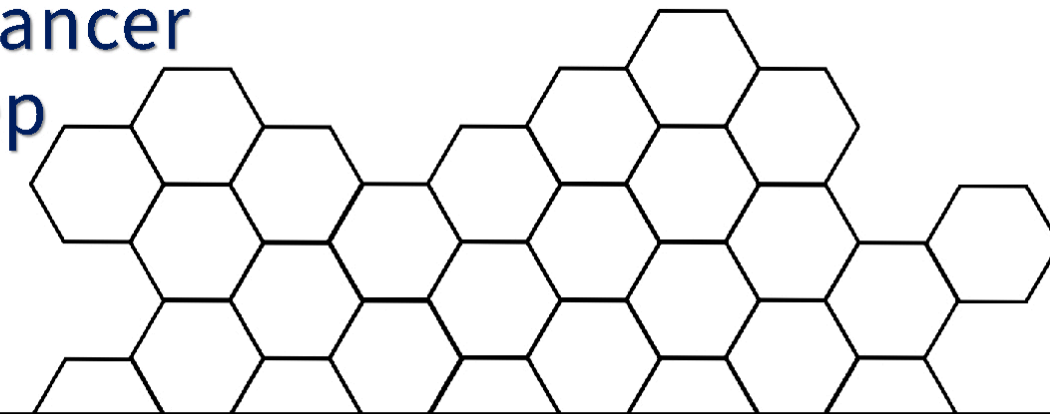# Detecting Pathological Complete Response in Esophageal Cancer after Neoadjuvant Therapy Based on Survival-weighted Deep Learning: A Pilot Study

S. CHENG[1], W. YAP[2] and E. TU[1]
(1) Taiwan AI Labs, Taipei, Taiwan
(2) Chang Gung Memorial Hospital, Taoyuan, Taiwan

INTRODUCTION

According to a recent meta-analysis, **24% to 32% of patients** with **esophageal cancer** reach a **pathological complete response (pCR)** after neoadjuvant radiochemotherapy (nRCT). For complete responders to nRCT, watchful-waiting approach instead of esophagectomy is currently under investigation. However, current image modalities seem to be insufficiently accurate to identify complete responders. Here, we introduce a **deep supervised learning** method leveraging a **survival-weighted loss function** to predict pCR while focusing on accuracy of subgroup with shorter progression-free survival (PFS).

AIM

This study aimed to predict pCR by developing a deep learning algorithm based on CT plan of neoadjuvant radiotherapy to guide the decision making of surgery.

METHOD

- All node-positive esophageal squamous cell carcinoma patients treated with nRCT followed by surgery between January 2014 and December 2017 are reviewed. Patients are categorized into pCR (ypT0/Tis ypN0) group and non-pCR group.
- A **dual-path DenseNet** model is trained on two channels of pixel data (planning CT and total dose map) for pCR prediction.
- The input of one path is GTV/CTV block in 3D shape for extracting pT features and the other input is whole slices in 2.5D shape for acquiring pN information.
- The loss function of cross-entropy is weighted by the value of customized PFS function w(s).

$$w(s) = \frac{1}{1+s} + \frac{1}{3} = \frac{s+4}{3s+3}$$

RESULTS

80 patients are included, of them 23 had pCR and 57 had non-pCR. Patient and tumor characteristics are summarized. 43 patients (53.75%) with shorter PFS than average (21.05 months) are stratified into high-risk subgroup. The dataset is randomly split into training-set (15 pCR + 41 non-pCR; 31 high-risk) and testing-set (8 pCR + 16 non-pCR; 12 high-risk). When survival-weighting is applied, the accuracy is 0.9167 (95% CI: 0.8979-0.9355) of high-risk subgroup versus 0.750 (0.7312-0.7688) of the others. When survival-weighting is not applied, the accuracy is 0.8333 (0.8079-0.8587) of high-risk subgroup versus 0.8333 (0.8101-0.8565) of the others.

Characteristics	Category	All patients (N=80), n (%)	pCR (N=23), n (%)	Non-pCR (N=57), n (%)	P
Sex	Male	76 (95)	20 (87.0)	56 (98.2)	0.04
	Female	4 (5)	3 (13.0)	1 (1.8)	
Age (year)	Mean (SD)	55.68±9.5	55.48±7.3	55.76±10.3	0.28
Location	Proximal	5 (8.9)	3 (13.1)	2 (6.1)	0.16
	Middle	23 (41.1)	12 (52.2)	11 (33.3)	
	Distal	28 (50)	8 (34.8)	20 (60.6)	
cT stage	cT2	10 (12.5)	2 (8.7)	8 (14.0)	0.67
	cT3	65 (81.2)	21 (91.3)	44 (77.2)	
	cT4	2 (2.5)	0 (0)	2 (3.5)	
	cT4a	3 (3.8)	0 (0)	3 (5.3)	
cN stage	N0	1 (1.3)	1 (4.3)	0 (0)	0.37
	N1	20 (25.0)	3 (13.1)	17 (29.8)	
	N2	43 (53.7)	15 (65.2)	28 (49.1)	
	N3	16 (20.0)	4 (17.4)	12 (21.1)	
cM stage	M1a	18 (22.5)	4 (17.4)	14 (24.6)	0.04
Clinical stage	II	5 (6.3)	2 (8.7)	3 (5.3)	0.70
	III	57 (71.2)	17 (73.9)	40 (70.1)	
	IVA, M1a	18 (22.5)	4 (17.4)	14 (24.6)	

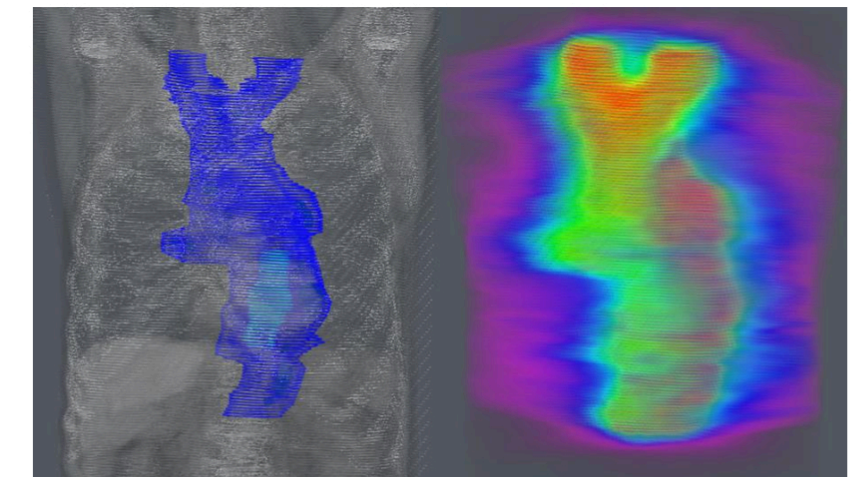Table 1: patients and disease characteristics

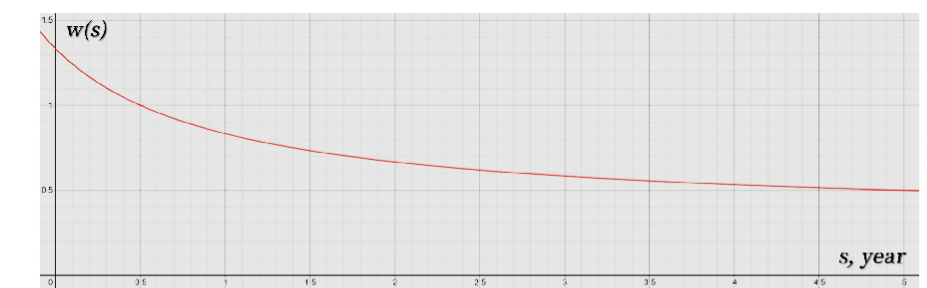Figure 1: CT plan and total dose map

Figure 2: customized PFS function w(s)

CONCLUSIONS

The accuracy of pCR prediction in shorter PFS subgroup is improved by survival-weighted learning without significant decrease in accuracy for the whole cohort.

REFERENCES

1. de Gouw DJJM, Klarenbeek BR, Driessen M, Bouwense SAW, van Workum F, Fütterer JJ, Rovers MM, Ten Broek RPG, Rosman C. (2019). Detecting Pathological Complete Response in Esophageal Cancer after Neoadjuvant Therapy Based on Imaging Techniques: A Diagnostic Systematic Review and Meta-Analysis. Journal of Thoracic Oncology, 14(7):1156-1171. https://doi.org/10.1016/j.jtho.2019.04.004
2. Soror, T., Kho, G., Zhao, K. L., Ismail, M., & Badakhshi, H. (2018). Impact of pathological complete response following neoadjuvant chemoradiotherapy in esophageal cancer. Journal of thoracic disease, 10(7), 4069–4076. https://doi.org/10.21037/jtd.2018.06.85
3. Hwang JS, Tsauo JY, Wang JD (1996). Estimation of expected quality adjusted survival by cross-sectional survey. Statistics in Medicine, 15;15(1):93-102. https://doi.org/10.1002/(SICI)1097-0258(19960115)15:1<93::AID-SIM155>3.0.CO;2-2
4. Liang, S., Zhang, R., Liang, D., Song, T., Ai, T., Xia, C., Xia, L., & Wang, Y. (2018). Multimodal 3D DenseNet for IDH Genotype Prediction in Gliomas. Genes, 9(8), 382. https://doi.org/10.3390/genes9080382

ACKNOWLEDGEMENTS

CONTACT INFORMATION

Shih-Chun Cheng
EMail: zheng.sq@ailabs.tw

長庚紀念醫院 Chang Gung Memorial Hospital

AI Labs.tw 台灣人工智慧實驗室