Double steps of deep learning algorithm decrease error in detection of lymph node metastasis in lung cancer patient

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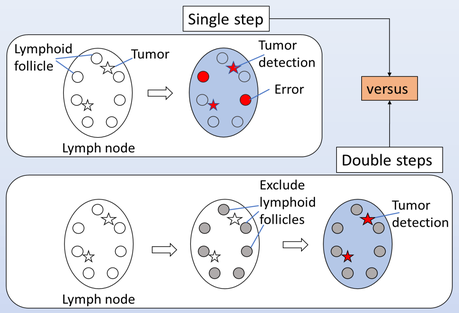
Background

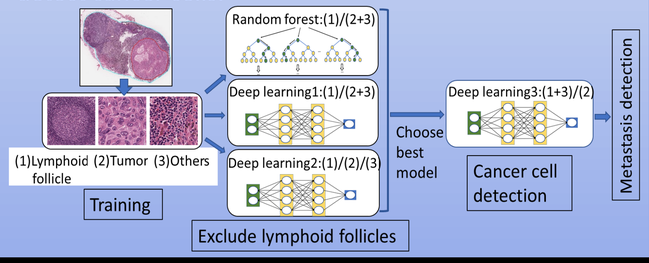
- Lymph node metastasis plays an important role to evaluate stages, treatment and prognosis of lung cancer.
- Using deep learning algorithm to detect metastasis in lymph nodes has attracted much attention but there are still errors due to cancer mimickers such as lymphoid follicles, macrophages.
- We hypothesized that using double steps deep learning including first step to exclude lymphoid follicles and second step to detect tumor, can reduce mistake and increase accuracy in detection of lymph node metastasis.

Methods

- 301 and 26 lymph node slides from Nagasaki University Hospital and Kameda Hospital of lung cancer patients were collected, respectively. In which, 224 slides (100 with, 124 without metastasis) were used for training set and 106 (49 with, 57 without metastasis) for testing set.
- Halo AI 2.2 ® software was used for this study.
- Evaluation of metastasis was based on whole-slide image level.
- We compared the analysed results between single step and double steps of deep learning algorithm.



- In first step, 3 models with different features were created for task of lymphoid follicle exclusion, then the best model was chosen.
- In second step, 1 more different model was built to detect cancer cells.



Results

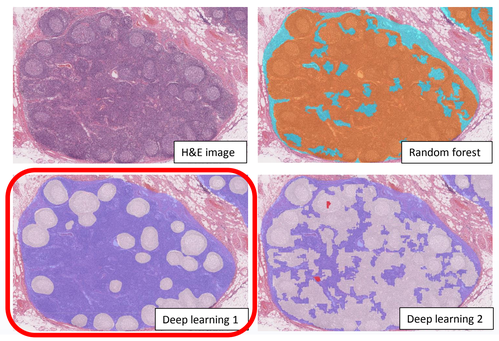


Figure 1. Selection of best model to detect lymphoid follicles . Deep learning 1 showed best result.

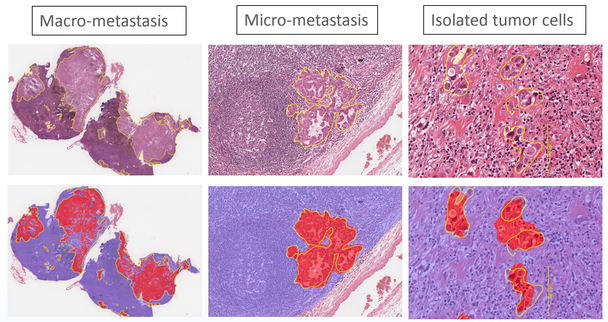


Figure 2. Double steps deep learning algorithm can detect variable size of tumor cells in metastatic slides. (*Red: tumor detection by AI, yellow line: annotation of tumor by pathologist as ground truth*)

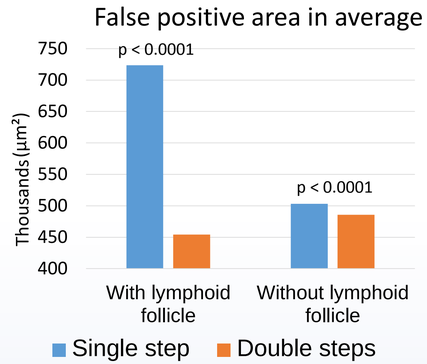


Figure 3. False positive area in average between groups with and without lymphoid follicles.

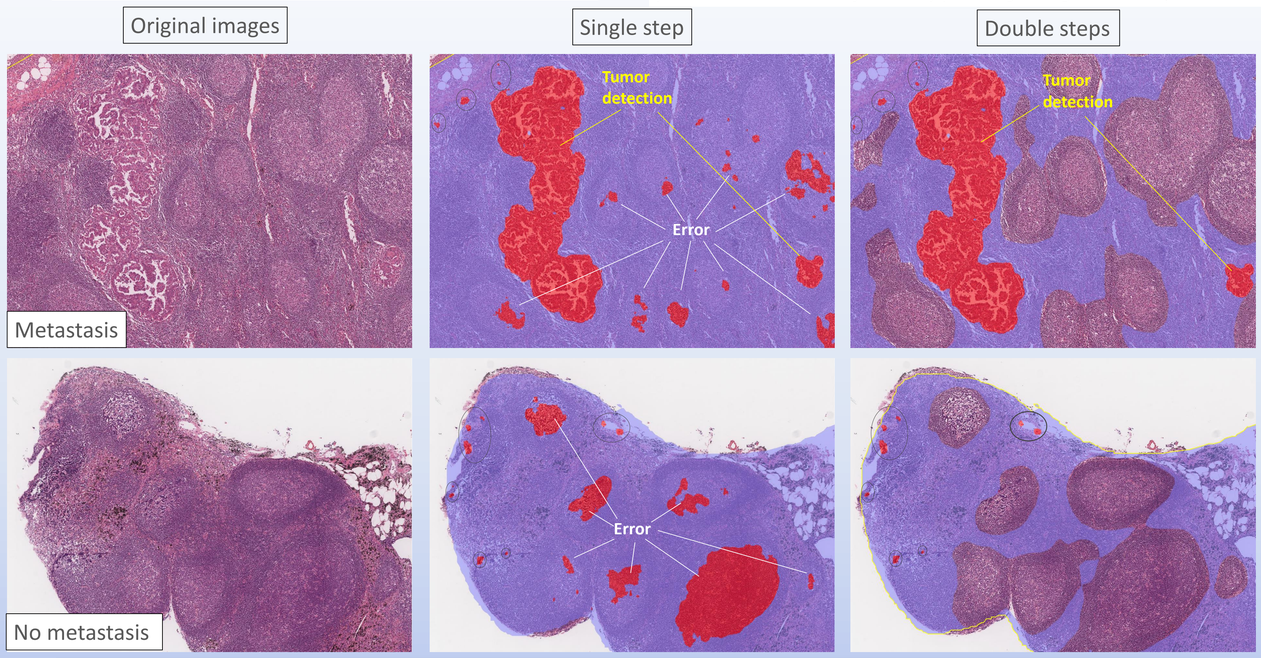


Figure 4. Reduction of false positive areas by double steps deep learning algorithm
(Black circle: remaining of some small false positive foci)

A

Max size of false positive foci (mm)	False positive rate on slide	Total of negative cases
> 1.1	0 (0%)	57 (100%)
> 1	1 (1.75%)	57 (100%)
> (0.7 - 0.9)	1 (1.75%)	57 (100%)
> 0.6	2 (3.5%)	57 (100%)

Table 1. Setting up cut-off point for remaining false positive foci in negative slides (A) and sensitivity, specificity in all data and using cut-off point (B).

B

	All original data	All data using cut-off point (1.1mm)
Sensitivity	100%	100%
Specificity	0	100%

Discussion

- In 3 models of first step, deep learning 1 showed best result to detect lymphoid follicles which was used as a filter to exclude error effectively in metastasis detection.
- Double steps deep learning algorithm can reduce up to 89% error compared to single step. There is a marked reduction in group with reactive lymphoid follicles, and slight reduction in group without reactive lymphoid follicles with statistical significance in both.
- Double steps deep learning can detect variable size of tumor cells in all metastatic slides with 100% sensitivity.
- Several small false positive foci remained in all negative slides due to fixed low threshold (50%) of tumor possibility causing low specificity in this study. By using cut-off point of 1.1mm for false positive region, we can detect no metastasis slides with adjusted high specificity.

Conclusion

- By using double steps of deep learning algorithm instead of single step, we can detect lymph node metastasis of lung cancer patient with significant reduction of error.
- Limitation of several remaining small false positive foci can be improved in next version of deep learning software.

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