Data-driven ex-vivo lung cancer detection using fibre-based fluorescence lifetime endomicroscopy

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Prothea TECHNOLOGIES

Background

Fluorescence lifetime imaging micro-endoscopy (FLIM): time-resolved images of autofluorescence signals, including intensity and lifetime.

FLIM-based cancer classification:

- lifetime contrast between healthy/unhealthy tissue based on the averaged lifetime with auxiliary knowledge.
- Conventional statistics-based methods: histogramming-based analysis

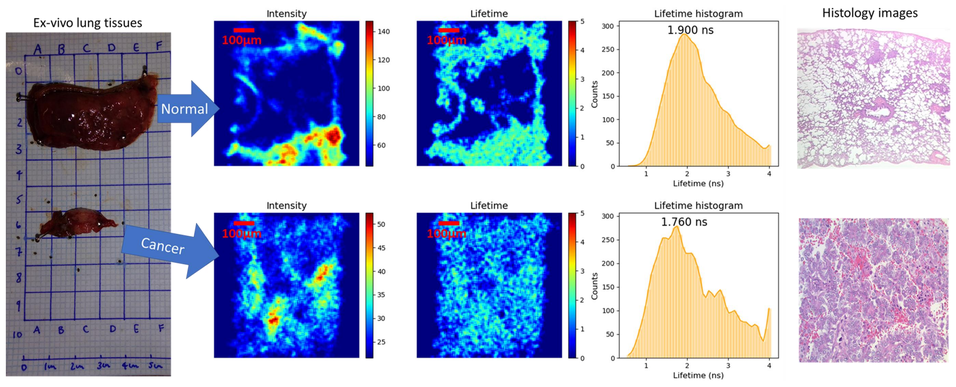

Figure 1. Contrast of the averaged lifetime (third column) of normal (first row) and cancerous (second row) lung tissue by histogramming lifetime images (second column) derived from intensity images (first column), along with histology images (fourth column) as the ground truth.[1]

Major challenges:

- Inter-patient heterogeneity: overlapping of lifetime ranges across patients
- Low-confidence lung cancer detection: 0.79 AUC (area under the ROC curve) [2]

Prothea Technologies Ltd:

- A spin-out from The University of Edinburgh and Bath
- With a vision of lung cancer diagnosis and treatment in a single hospital visit
- In-vivo molecular imaging using KronoScan (Figure 3) through optical fibres (Figure 2)
- AI-integrated real-time in-procedure detection to support clinical decision-making

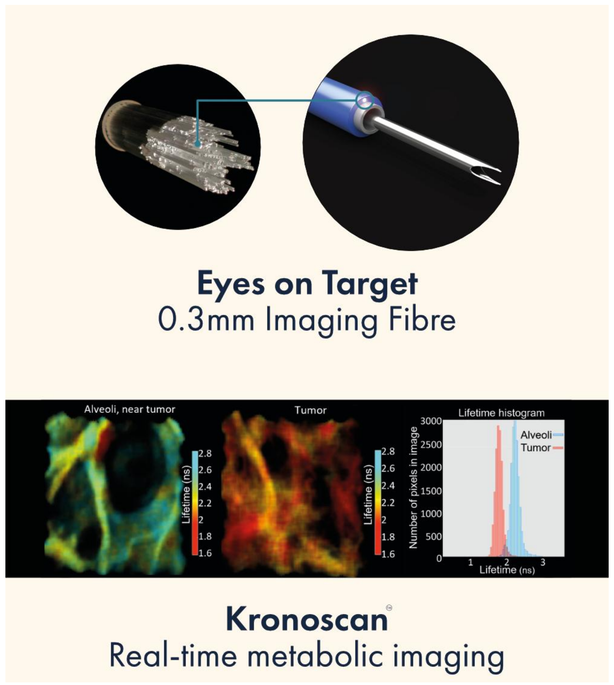

Figure 2. Our bespoke Eye on Target optical fibre for in-vivo imaging.

Figure 3. Our next-generation fibre-based FLIM system, namely KronoScan.

Methodology

Data collection:

- Cohort: pairs of ex-vivo normal and cancer tissue from 21 patients
- KronoScan imaging: 128*128 images at ~9 FPS with multiple exposure times (primarily 6 and 20 μs) at multiple physical measuring points on each tissue
- Ground truth: the corresponding histology images were annotated by a pathologist as the ground truth
- Lifetime reconstruction: rapid lifetime determination of 2-time bins

Image pre-processing:

- Denoising, normalisation, contrast enhancement, and masking.[1,3]
- Different formatting/stacking of the post-processed images (Figure 4) [3]:
  - Greyscale/pseudo-colour lifetime images
  - Stacked FLIM images: intensity and lifetime as two channels in an RGB image, with the remaining channel as zeros.
  - Intensity-weighted lifetime images: intensity as the soft weight to the pseudo-colour lifetime images

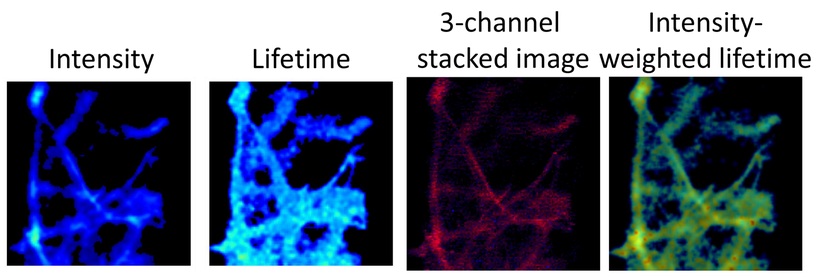

Figure 4. 3-channel stacked image (third) and intensity-weighted lifetime image (fourth) by intensity (first) and lifetime (second) image.[3]

Models: from conventional ML to custom DL architectures

- Conventional ML methods: K-nearest neighbours, support-vector machine, artificial neural networks, and random forest
- Conventional DL methods: ResNet, ResNeXt, DenseNet, Inception, and Xception
- Custom DL architectures:
  - Hierarchically aggregated multi-scale models
  - Vanilla and dilated convolutions
  - Aggregation by Addition or Concatenation

Metrics

- Accuracy, precision, recall, area under the receiver operating characteristic (ROC) curve (AUC), etc.
- TP: true positive; TN: true negative; FP: false positive; FN: false negative

$$Accuracy = \frac{TP + TN}{TP + FP + TN + FN} \qquad Precision = \frac{TP}{TP + FP} \qquad Recall = \frac{TP}{TP + FN}$$

Results

*Table 1. Performance of various ML/DL models. CNN: convolutional neural networks. MSAD: Multi-Scale Aggregated Dilated Networks. W: width of the networks. S: scale of the networks. The best scores are in **bold**.*

	Accuracy	Precision	Recall	AUC
Conventional ML methods (pixel lifetime values) [4]				
KNN	0.613	0.563	0.559	0.608
SVC	0.767	0.734	0.742	0.765
NN	0.763	0.722	0.752	0.761
RF	0.778	0.83	0.627	0.763
Conventional CNN models (stacked images/intensity-weighted lifetime) [2]				
ResNet50	0.828/0.836	0.83/0.894	0.893/0.7714	0.813/0.8375
DenseNet	0.785/0.830	0.824/0.891	0.812/0.7624	0.779/0.832
Inception	0.794/0.825	0.838/0.884	0.812/0.742	0.79/0.850
Xception	0.769/0.811	0.854/0.782	0.739/0.876	0.777/0.809
Multi-Scale Aggregated Dilated Networks (stacked images) [5]				
MSAD-W16-S6	**0.878**	0.874	**0.929**	**0.866**
MSAD-W24-S4	0.865	0.892	0.879	0.861
MSAD-W32-S2	0.876	0.876	0.922	0.865
ResNetZ (intensity-weighted lifetime) [3]				
ResNetZ50-W12-S2	0.828	0.875	0.777	0.830
ResNetZ50-W16-S2	0.858	0.872	0.847	0.858
ResNetZ50-W12-S4	0.860	**0.916**	0.802	0.862
ResNetZ50-W16-S4	0.833	0.864	0.801	0.834

Conclusions

- ML/DL-based automated classification: superior to statistics-based methods
- ML methods are inferior to DL methods
- Intensity-weighted lifetime images: more suitable for the CNN models
- More advanced CNN architectures (MSAD and ResNetZ) with better performance, but models with further wider and more scales not resulting in further improved metrics
- Intensity-weighted lifetime outperformed other formats for the classification
- Future work focusing on in-vivo detection via our ongoing clinical trials.

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