

Artificial intelligence-based bone marrow cell classification

臺大醫院檢驗醫學部 周文堅 June 20, 2020

Outlines

- AI-based blood cell classification
- NTUH x aether AI: bone marrow cell classification project
- Conclusion
- Q&A

AI-based blood cell classification

AI-based blood cell classification:

An important and popular issue

Year	Title & Journal	Blood
2007	Morphological Granulometric Features of Nucleus in Automatic Bone Marrow White Blood Cell Classification IEEE Trans Inf Technol Biomed.	BM
2014	A Neural-Network-Based Approach to White Blood Cell Classification ScientificWorldJournal	PB
2015	Segmentation and Classification of Bone Marrow Cells Images Using Contextual Information for Medical Diagnosis of Acute Leukemias PLoS One.	BM (leukemia only)
2019	A Novel Automated Image Analysis System Using Deep Convolutional Neural Networks Can Assist to Differentiate MDS and AA Sci Rep	PB
2019	Deep Learning Approach to Peripheral Leukocyte Recognition PLoS One	PB

AI-based blood cell classification

An unmet clinical need. No mature model has been developed.

Year	Title & Journal	Blood						
2019	Simultaneous Cell Detection and Classification in Bone Marrow Histology							
	IEEE J Biomed Health Inform	(biopsy)						
2019	Recognition of Peripheral Blood Cell Images Using Convolutional Neural Networks							
	Comput Methods Programs Biomed							
2020	Machine-Based Detection and Classification for Bone Marrow Aspirate Differential Counts: Initial Development Focusing on Non-Neoplastic Cells Lab Invest.	BM						
2020	White Blood Cells Detection and Classification Based on Regional Convolutional Neural Networks	PB						
	Med Hypotheses							

Problems of the previous studies

- Limited parameters of training
- Limited cell categories for AI identification
- Limited numbers of cells for training (< 200 cells)
- PB (peripheral blood), rather than marrow
- Leukemia only
- Non-neoplastic cells only

-- Comprehensive, including both normal and neoplastic cells

-- Advanced, marrow, which contains complicated background and cell categories

-- Intensive, much more cells are needed for AI training



-- Experts reading marrow

-- Competent AI team

Unmet need : bone marrow cell classification and counting

Manual counting of bone marrow (BM) blood cells

- Essential for hematologic diagnosis
- Time consuming, high inter-observer variation





NTUH x aether AI: bone marrow cell classification project

Difficulties of training AI with marrow blood

- 1. Marrow blood is much less available than peripheral blood
- 2. Cells are **crowded** in marrow blood
- 3. Background is complex in marrow blood
- 4. More types of leukocytes to be identified in marrow blood
- 5. Oil objective lens (100x) are usually required
- 6. Multidisciplinary experts requirement: leukocyte morphology, AI

training





NTUH + aether AI

1+1 > 2

Team	Advantages						
NTUH	Huge data set of BM smears Experts in clinical hematology and cytology						
aether Al	Experts in AI model tranining, computer science and data management.						



Create an automatic approach of BM cell classification







Retrospective dataset

NTUH: National Taiwan University Hospital AML: acute myeloid leukemia CML: chronic myeloid leukemia

BM smear slides from NTUH (stained with Liu's stain)

Images taken manually at 1000X magnification (oil lens)



AML (Liu's stain)

CML (Liu's stain)

Method



Results: annotated slides

Hematologic disease	Number
Acute myeloid leukemia	109
Acute lymphoblastic leukemia	33
Mixed phenotypic acute leukemia	4
Myelodysplastic syndrome (MDS)	24
Myeloproliferative neoplasm (MPN)	17
MDS/MPN	22
Chronic lymphocytic leukemia	3
Adult T-cell leukemia/lymphoma	2
Plasma cell neoplasm	34
Hodgkin lymphoma	4
Aggressive non-Hodgkin lymphoma	81
Indolent non-Hodgkin lymphoma	37
Aplastic anemia/pure red cell aplasia	16
Idiopathic thrombocytopenic purpura	7
Eosinophilia	2
Mastocytosis	2
Langerhans cell histiocytosis	1
Hemolytic anemia	6
Infectious etiology	14
Solid cancer with bone marrow involvement	17
Cytopenia with no identified etiology	6

2018/05 to 2020/04/27

441 BM smears 17546 Images

Results: annotated cell numbers

Cell Types	Train	Test	Total
Blast	20627	2719	23346
Promyelocyte	15788	643	16431
Neutrophilic-myelocyte (Myelocyte)	28034	1005	29039
Neutrophilic-metamyelocyte (Metamyelocyte)	20333	698	21031
Neutrophilic band + Segmented neutrophil (PMN)	74763	2662	77422
Eosinophil-and-precursor	9148	548	9696
Basophil	1789	155	1944
Monocyte-and-precursor	12092	792	12884
Lymphocyte	38127	2286	40413
Plasma-cell	8307	74	8381
Erythroid-lineage-cell (Erythroid)	61888	2938	64826
Mitosis	2123	141	2264
Histiocyte	1355	220	1575
Invalid	110264	4422	114686
Total			423938

Test set: labeled by expert



Test set: labeled by Al



Results: accuracy confusion matrix

															Gold standard
Confusion Matrix, Accuracy=0.936									Ψ						
2														100.0% 2/2	-BG
	23										14			62.2% 23/37	Basophil
2		767		12		50			15		1		З	90.2% 767/850	Blast
2			386					1		5	1		1	97.5% 386/396	-Eosinophils-and-precursors
2				805		1								99.6% 805/808	Erythroid
					23				З			1		85.2% 23/27	Histiocyte
1		13		25		323			8			11	1	84.6% 323/382	-Lymphocyte
1			1				138			4	29			79.8% 138/173	Metamyelocyte
			1					64				2		95.5% 64/67	Mitosis
		2		1		5	2		102		8			85.0% 102/120	Monocyte-and-precursors
2							12			406			2	96.2% 406/422	Myelocyte
1							6	1			1099			99.3% 1099/1107	PMN
				1								33		97.1% 33/34	-Plasma-cell
		6							7	27			134	77.0% 134/174	-Promyelocyte
15.4% 2/13	100.0% 23/23	97.3% 767/788	99.5% 386/388	95.4% 805/844	100.0% 23/23	85.2% 323/379	87.3% 138/158	97.0% 64/66	75.6% 102/135	91.9% 406/442	95.4% 1099/1152	70.2% 33/47	95.0% 134/141		-Precision
BG	Basophil -	Blast -	nd-precursors	Erythroid	Histiocyte -	Lymphocyte -	etamyelocyte -	Mitosis -	nd-precursors -	Myelocyte -	MMA	Plasma-cell -	Promyelocyte -	Recall	
			Eosinophils-a			Al p	≥ redicti	on	Monocyte-a		Precision(精確率):機器判斷是A細胞,則此細胞真為A細胞的機率 Recall(召回率):資料中有100顆A細胞,機器能夠找出幾顆A細胞				

Ground Truth

Milestones in this project



Clinical validation in multi-centers



Multicenter clinical validation



Video demo

https://youtu.be/XxyyBmcmBkU



Conclusion

Recent advances in deep learning: AI-based medicine becomes real

NTUH x aether AI project:

A model of industry-academia-research cooperation

Largest AI-based BM cell classification model in the world

Promising initial result

Ongoing multicenter clinical validation

Hope this automatic BM cell classification model would become clinically useful and available in the near future

Acknowledgement



Questions or comments