

OBJECTIVES

Our study objectives are as follows:

- 1) Presenting a comprehensive, systemically categorized, and manually annotated cell-level benchmark dataset for Ki-67 expression in breast cancer.
- 2) Assessing the current lack of domain-specific benchmark resources in the field and enables rigorous evaluation of automatic Ki-67 quantification tools.
- 3) Supporting patient safety and promote the responsible adoption of automated solutions in clinical practice.

INTRODUCTION

Ki-67 proliferation index serves as a pivotal prognostic and predictive marker in breast cancer pathology [1]. Due to its high inter-observer variability and the labor-intensive nature of its measurement [2], numerous automated quantification tools for Ki-67 have been developed. However, as few benchmark datasets are available [3], most of these tools lack rigorous validation in clinical settings. To address this, we constructed QuaCCa-BRS Ki-67, a cell-level dataset for Ki-67, covering diverse histologic patterns including tumor, non-tumor and miscellaneous scenarios in breast cancer.

METHODS

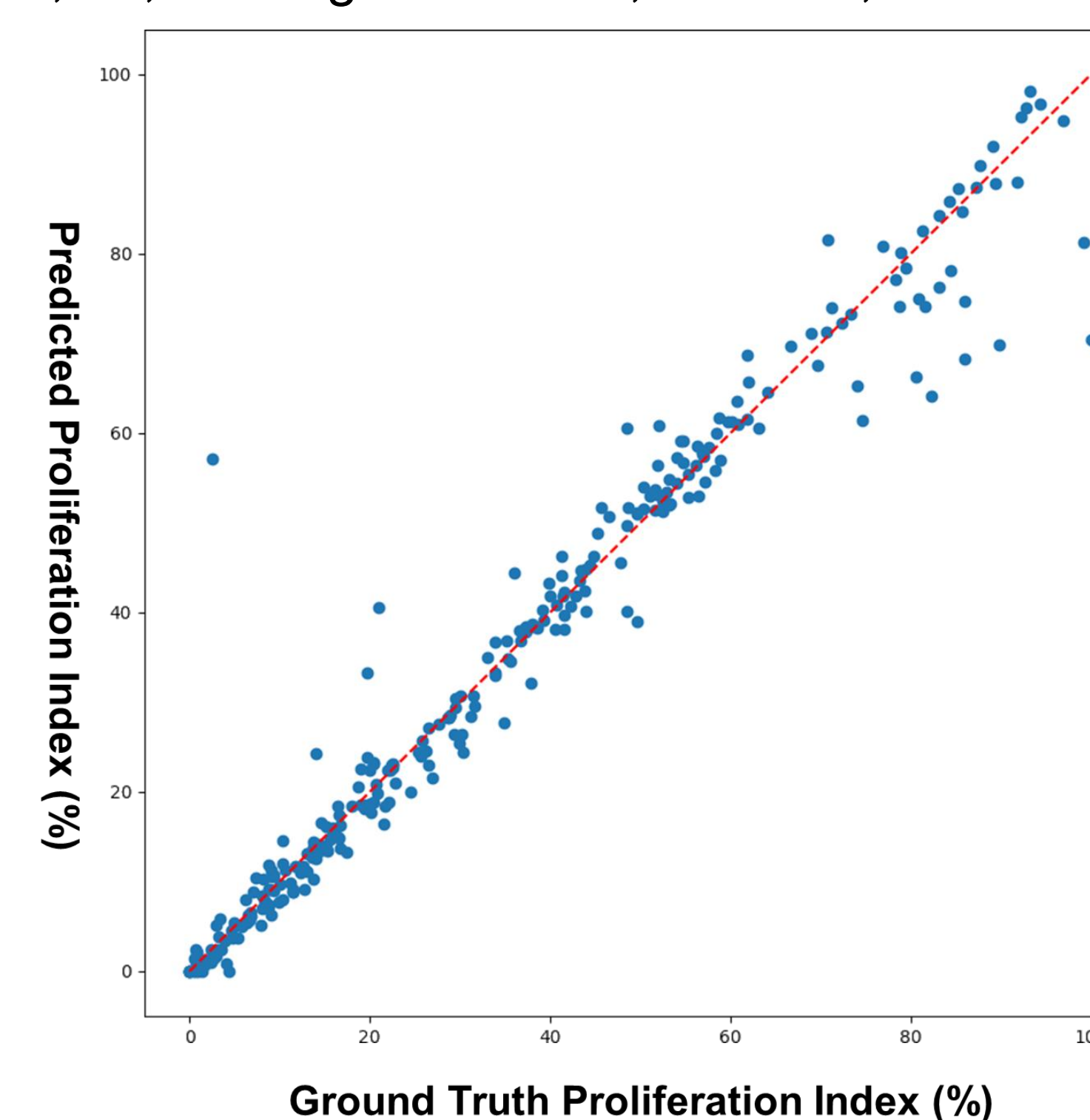
A total of 104 Ki-67 slides from breast cancer patients were collected from Korea University Guro Hospital and scanned using a Philips SG300 scanner at 40× objective magnification. For systematic classification, three main categories—tumor, non-tumor and miscellaneous—were defined. The tumor category was subdivided based on growth pattern and dichotomized by Ki-67 expression level ($\geq 25\%$ vs. $< 25\%$). The non-tumor category included precursor, benign, and reactive lesions, as well as normal breast tissue. Non-cellular regions and artifacts were grouped under the miscellaneous category. For each subcategory, image patches matching the definitions were selected and cropped to 1024 × 1024 pixels in size. Finally, every cell was manually annotated as a positive tumor cell, negative tumor cell, or non-tumor cell.

RESULTS

Table 1. Categories and Subcategories of QuaCCa-BRS Ki-67

Category	Subcategory	Ki-67 Expression Level	Subcategory		
			Subcategory	Subcategory	
Tumor	Invasive	Tubular-Low	Non-tumor	Precursor	Atypical glands
		Tubular-High			Columnar cell change (CCC)
		Glandular-Low			Fibroadenoma (FA) / Fibroadenomatous change
		Glandular-High			Fibrocystic change (FCC)
		Solid-Low			Lobular carcinoma in situ (LCIS)
		Solid-High			Sclerosing adenosis (SA)
		Cribriform-Low			Usual ductal hyperplasia (UDH) / Intraductal papilloma (IDP)
		Cribriform-High			Foreign-body reaction
		Nested-Low			Macrophage
	Nested-High	Lymphocytes			
	Mucinous-Low	Germinal center			
	Mucinous-High	Simple duct			
	Lobular-Low	Complex duct			
	Lobular-High	Terminal ductal lobular unit (TDLU)			
	Papillary & Micropapillary	Small vessel			
	Uncommon	Large vessel			
	DCIS	Cribriform	Normal	Blood (RBC)	
		Solid		Skeletal muscle	
		Comedo		Smooth muscle	
Miscellaneous	Miscellaneous	Artifact		Nerve	
		Necrosis		Adipocyte	
		Ink		Skin epidermis	
		Shadow		Skin adnexa	
		Blank		Stroma	

The tumor, non-tumor, and miscellaneous categories had 19, 23, and 5 subcategories, respectively. For each subcategory, 15 patches were selected for tumor subcategories and 10 patches were selected for non-tumor and miscellaneous subcategories. In total, 585 image patches were collected and 226,080 cells were annotated (32,667 positive tumor, 63,710 negative tumor, and 129,703 non-tumor cells).



Using the QuaCCa-BRS Ki-67 dataset, Qanti IHC, trained with independent data, achieved $mAP@50-95 = 0.873$ and showed very strong correlation between predicted and ground truth Ki-67 proliferation indices (Pearson correlation coefficient = 0.979; $p < 0.001$).

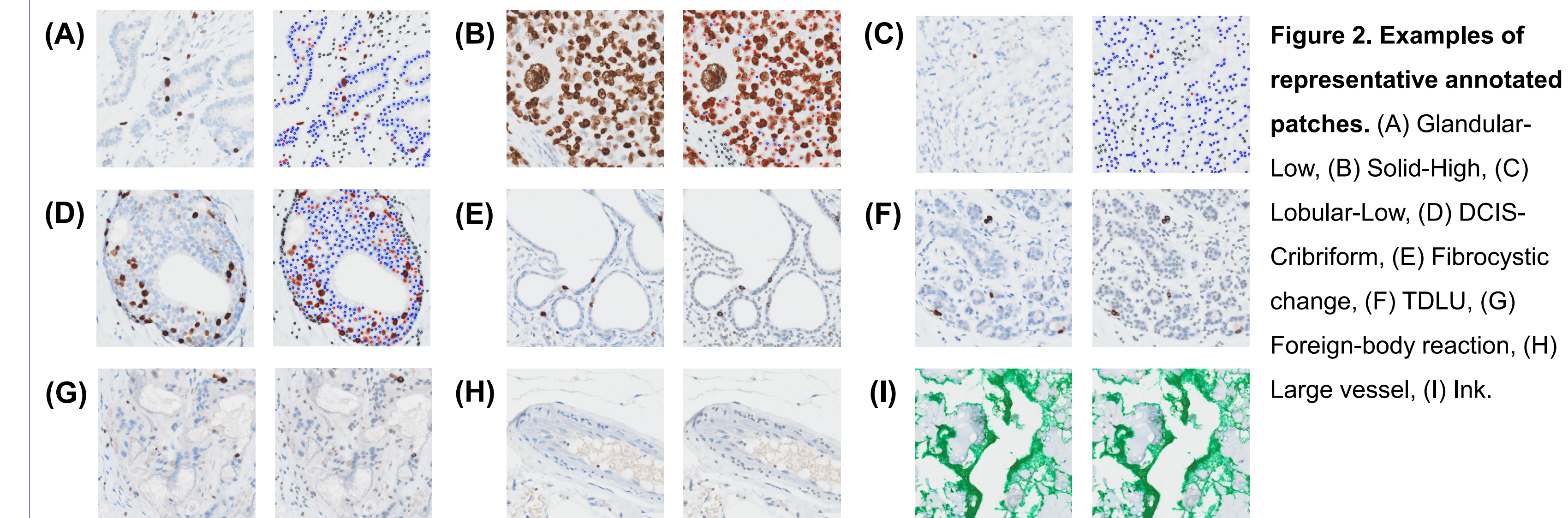


Figure 2. Examples of representative annotated patches. (A) Glandular-Low, (B) Solid-High, (C) Lobular-Low, (D) DCIS-Cribriform, (E) Fibrocystic change, (F) TDLU, (G) Foreign-body reaction, (H) Large vessel, (I) Ink.

CONCLUSIONS

We present a comprehensive, systematically categorized, and manually annotated cell-level dataset for Ki-67 in breast cancer, capturing diverse histologic patterns, expression levels, and cell types. QuaCCa-BRS Ki-67 addresses the current lack of domain-specific benchmark resources in the field and enables rigorous evaluation of Ki-67 quantification tools. By facilitating robust validation, it will support patient safety and promote the responsible adoption of automated solutions in clinical practice.

REFERENCES

- [1] Nielsen TO, Leung SCY, Rimm DL, et al. Assessment of Ki67 in breast cancer: updated recommendations from the International Ki67 Working Group. *JNCI J Natl Cancer Inst.* 2021;113(7):808-819. doi:10.1093/jnci/djaa201.
- [2] Chung, Yul Ri et al. "Interobserver Variability of Ki-67 Measurement in Breast Cancer." *Journal of Pathology and Translational Medicine* 50 (2016): 129 - 137.
- [3] Huang, Zhongyi et al. "BCData: A Large-Scale Dataset and Benchmark for Cell Detection and Counting." *International Conference on Medical Image Computing and Computer-Assisted Intervention* (2020).

DATA AVAILABILITY / CONTACT

The dataset in this work will be available upon reasonable request after publication of the paper. Please contact the first, corresponding author, or info@aivis.kr for more information.

