Yves Sucaet Wim Waelput

Digital Pathology



SpringerBriefs in Computer Science

Series editors

Stan Zdonik, Brown University, Providence, USA
Shashi Shekhar, University of Minnesota, Minneapolis, USA
Jonathan Katz, University of Maryland, College Park, USA
Xindong Wu, University of Vermont, Burlington, USA
Lakhmi C. Jain, University of South Australia, Adelaide, Australia
David Padua, University of Illinois Urbana-Champaign, Urbana, USA
Xuemin (Sherman) Shen, University of Waterloo, Waterloo, Canada
Borko Furht, Florida Atlantic University, Boca Raton, USA
V.S. Subrahmanian, University of Maryland, College Park, USA
Martial Hebert, Carnegie Mellon University, Pittsburgh, USA
Katsushi Ikeuchi, University of Tokyo, Tokyo, Japan
Bruno Siciliano, Università di Napoli Federico II, Napoli, Italy
Sushil Jajodia, George Mason University, Fairfax, USA
Newton Lee, Newton Lee Laboratories, Tujunga, USA



Yves Sucaet · Wim Waelput

Digital Pathology



Yves Sucaet Wim Waelput Pathomation Berchem Belgium

ISSN 2191-5768 ISBN 978-3-319-08779-5 DOI 10.1007/978-3-319-08780-1 ISSN 2191-5776 (electronic) ISBN 978-3-319-08780-1 (eBook)

Library of Congress Control Number: 2014943501

Springer Cham Heidelberg New York Dordrecht London

© The Author(s) 2014

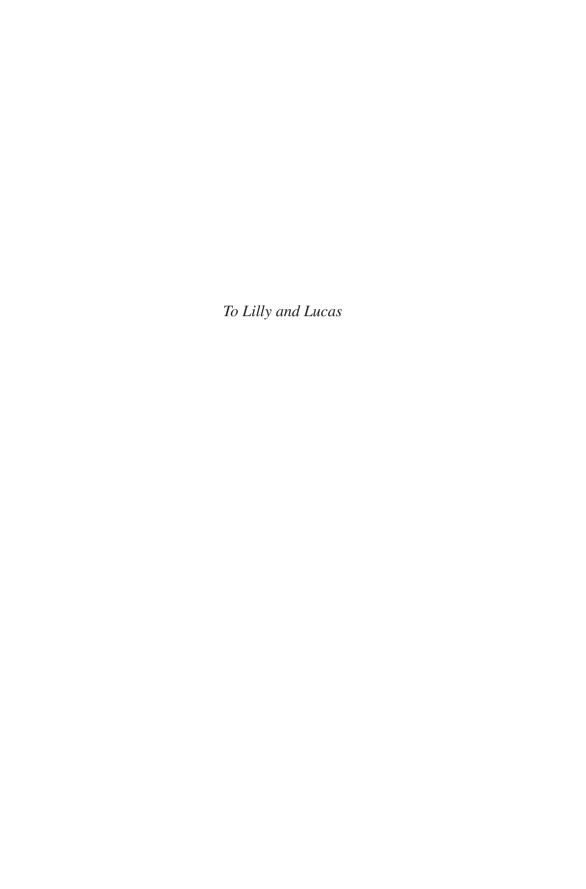
This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed. Exempted from this legal reservation are brief excerpts in connection with reviews or scholarly analysis or material supplied specifically for the purpose of being entered and executed on a computer system, for exclusive use by the purchaser of the work. Duplication of this publication or parts thereof is permitted only under the provisions of the Copyright Law of the Publisher's location, in its current version, and permission for use must always be obtained from Springer. Permissions for use may be obtained through RightsLink at the Copyright Clearance Center. Violations are liable to prosecution under the respective Copyright Law.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

While the advice and information in this book are believed to be true and accurate at the date of publication, neither the authors nor the editors nor the publisher can accept any legal responsibility for any errors or omissions that may be made. The publisher makes no warranty, express or implied, with respect to the material contained herein.

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)



Preface

Dr. Sucaet holds a Ph.D. in Bioinformatics from Iowa State University. His research background is in systems and network biology. He is a co-founder of Pathomation and currently fulfills the role of Chief Technology Officer. Before that, he was at HistoGeneX in the function of Section Head, Data Management and Bioinformatics, where he met Dr. Waelput. They decided to combine their expertise and have been promoting the use of digital pathology ever since.

Dr. Waelput is an M.D. and certified pathologist, currently employed as a senior staff member at the University Hospital of Brussels (UZ-Brussels). He is also a consulting (pharma-)pathologist at HistoGeneX and a co-founder of Pathomation. Dr. Waelput has been involved in research on protein–protein interactions and signal transduction within the Department of Medical Protein Research at the Flemish Institute for Biotechnology (VIB—Vlaams Instituut voor Biotechnologie). He obtained his Ph.D. from the University of Ghent.

Pathomation is a young innovative company founded in 2012. The company was created by two pathologists and a bioinformatician. Located in Berchem, Belgium, the company strives to offer the most comprehensive software platform for digital pathology possible. The focus is on integration, scalability, and userfriendliness. Pathomation implements digital pathology in a variety of use cases and scenarios. Truly vendor-independent digital pathology solutions are hard to come by. Platforms that claim to be vendor-independent are difficult to adapt to specific circumstances. Interoperability, which is taken for granted in wet lab conditions (e.g., a sample is sectioned on a Leica microtome, stained on a Dako autostainer, and studied under an Olympus microscope), is often lacking when moving to digital pathology. Therefore, Pathomation develops software for pathologists, designed by pathologists. Its PathoCore software can read most proprietary vendor formats, so the company is not tied to any technology and can offer objective guidance. PathoCore is central to a complete software platform. In addition, other applications are available, including viewers and host application plug-ins. Because of this component-based architecture, Pathomation is ideally placed to take digital pathology information (including augmented datasets like on-slide annotations and captured form-data) and deliver it to any target environment or device.

viii Preface

This work would not have been possible without the valuable input of several others. We would like to thank, in alphabetical order:

David Ameisen Essam E. Ayad Peter Lang Zev Leifer Mathieu Malaterre Koen Marien Agelos Pappas Yukako Yagi

And a special thank you to Simon Rees and Wayne Wheeler of Springer for guiding us through the publishing process.

Contents

1	Digi	tal Pathology's Past to Present	1
	1.1	Introduction	1
	1.2	Beginnings and Evolution	3
		1.2.1 Reaching Out: Telepathology Networks	4
		1.2.2 Digital Pathology and Whole Slide Imaging	5
		1.2.3 Differences with Radiology	7
	1.3	Successes and Challenges	8
	1.4	Digital Pathology Today	9
	1.5	Preliminary Conclusions	10
	Refe	erences	10
2	Har	dware and Software	15
	2.1	How Are Digital Pathology Images "Captured"?	15
	2.2	How Do Slide Scanners Work?	17
	2.3	Virtual Slide Formats	20
		2.3.1 How Are WSI Data Organized?	20
		2.3.2 The Pyramidal Format	20
		2.3.3 Tiles	20
		2.3.4 Color Spaces	21
		2.3.5 Compression Schemes	22
	2.4	Vendor-Specific File Format Implementations	22
		2.4.1 TIFF-Based Formats.	22
		2.4.2 Other Format Types	25
		2.4.3 The Role of DICOM.	27
	2.5	Bits, Bytes, and Wires	27
		prences	28
3	App	lications	31
-	3.1	Education	31
	3.2	Remote Consultations and Second Opinions	33
	3.3	Tumor Boards and Pathology Reviews	34
	2.2		

x Contents

	3.4	Biobanking and Collection Hosting	35
	3.5	Primary Diagnosis	38
		3.5.1 In the USA: The Role of the FDA	38
		3.5.2 Throughout the Rest of the World	39
	3.6	Birds of a Feather	40
	Refe	rences	40
4	T	and Anna Tarasta	12
4		ge Analysis	43
	4.1	Current Technology and Challenges	43
	4.2	Current State of Digital Pathology and WSI Analysis	48
	4.3	Toward In Silico Pathology	50
	Refe	rences	50
5	Ugo	Conn	57
3		Cases	
	5.1	Diagnosis and Staging of Disease	57
		5.1.1 Biomarkers	57
		5.1.2 Cytology	60
	5.2	Digital Pathology as a Teaching Tool	62
		5.2.1 New York College of Podiatric Medicine	62
		5.2.2 Universal Education	63
	5.3	Telepathology in Developing Countries	64
		5.3.1 E-Education and Telepathology in Egypt	65
		5.3.2 Heavy Lifting in Port-au-Prince, Haiti	66
	5.4	Quality Control and Assurance	67
	5.5	Tremendous Potential	68
	Refe	rences	69
,	A D	wight France	71
6		right Future	71
	6.1	The 5 %/\$2.4 Billion Challenge	71
	6.2	New Frontiers	72
		6.2.1 Medical Systems Biology	72
		6.2.2 Three-Dimensional WSI	73
		6.2.3 Spectral Imaging	74
		6.2.4 Extending the Pathology Value Chain, Upstream,	
		and Downstream	75
	6.3	Hope for the Third World	76
	6.4	Digital Pathology DIY	77
	6.5	Final Conclusions	78
	6.6	Learn More About Digital Pathology	78
	Refe	rences	79
Re	tract	ion Note: Hardware and Software	E1
Al	out 1	he Authors	81
In	dev		83

Chapter 1 Digital Pathology's Past to Present

Abstract Digital pathology is a rapidly growing field that did not even exist 20 years ago. However, in some ways, its origins date back to the earliest attempts at telepathology back in the 1960s. This chapter provides a brief historical perspective on how digital pathology came to be. It answers questions like why does it exist and what need does it fulfill? It also provides a brief summary of current applications and the challenges ahead; explains why we believe digital pathology is rapidly coming of age; and describes the converging factors that lead us to this conclusion.

Keywords Digital pathology · Digital pathology history · Telepathology · Informatics · Whole slide imaging · Pathology cockpit · Pathology dashboard · WSI · DP

1.1 Introduction

One of the world's most renowned and successful inventors, the late Charles Franklin Kettering (1876–1958), also was a very gifted man of words. Among his most famous lines are: "Our imagination is the only limit to what we can hope to have in the future" and "People are very open-minded about new things—as long as they're exactly like the old ones." These two statements encapsulate the struggles that exist with any novel idea, and certainly with any new field, whether that field is in engineering, science, art, or medicine.

Among the very newest of fields in medicine is the field of digital pathology which, as a distinct entity, only started to be mentioned in published, peer-reviewed scientific journals in the year 2000 [1–3], though its roots reach at least into the 1990s [4] and perhaps even further. Initially, relatively little was written about digital pathology; but this has changed dramatically, especially over the