



DEVELOPING THE QUALITY CULTURE IN ANATOMICAL PATHOLOGY

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WHY HAS INTRODUCTION OF QUALITY PROGRAMS BEEN SO SLOW IN ANATOMICAL PATHOLOGY LABORATORIES?

- \$\$\$\$
- VARIABILITY IN TECHNICAL ASPECTS OF TISSUE PROCESSING
- INTER-OBSERVER (AND INTRA-OBSERVER) VARIABILITY IN DIAGNOSES BY EXPERT PATHOLOGISTS

SOME BREAST CANCER STATISTICS IN BRITISH COLUMBIA

- THE NUMBER OF INVASIVE BREAST CANCER CASES DIAGNOSED IN 2005 WAS 2705 (645 IN VCH) (1 IN 9 LIFETIME RISK FOR WOMEN)
- THE 5 YEAR SURVIVAL RATE FOR BC WOMEN DIAGNOSED WITH BREAST CANCER IN YEAR 2000 WAS 89% (IN 1970 THIS RATE WAS 60-70%)

BREAST CANCER SURVIVAL STATISTICS ARE BETTER TODAY BECAUSE:

- EARLIER DIAGNOSIS
- MORE ACCURATE DIAGNOSIS
- BETTER STANDARD CHEMOTHERAPY
- SPECIALIZED THERAPY TAILORED TO SPECIFIC BREAST CANCER SUBTYPES BASED ON ER, PR, AND HER-2 TESTING

When treatment is based on immunostaining results, everything changes!

THE CHALLENGE- HOW DO WE ASSURE THAT ER/PR/HER-2 TESTING IN B.C. IS ACCURATE?

- 11 LABORATORIES IN BC PERFORM IHC FOR BREAST CARCINOMA MARKERS
- MULTIPLE METHODS AND DETECTION SYSTEMS
- MULTIPLE PATHOLOGISTS INTERPRETING TEST RESULTS
- RESULTS MUST BE BOTH SENSITIVE AND SPECIFIC
 - A FALSE NEGATIVE ER/PR/HER-2 TEST COULD DENY LIFE-SAVING TREATMENT
 - A FALSE POSITIVE HER-2 TEST EXPOSES PATIENT TO POSSIBLE DRUG TOXICITY AND COSTS THE HEALTH CARE SYSTEM \$40,000 PER YEAR FOR THE REMAINDER OF PATIENT'S LIFE


QUALITY ASSURANCE: HOW DO WE ASSURE THAT ALL BC LABS ARE TESTING PROPERLY?

- MANDATE ER/PR/HER-2 TESTING ON ALL BREAST CARCINOMAS
- MANDATE STANDARDIZED FIXATION OF ALL BREAST CANCER SPECIMENS
- MANDATE THAT ALL LABS MONITOR ER/PR/HER-2 POSITIVITY RATES TO DETECT VARIATION FROM PROVINCIAL AND NATIONAL MEANS
- MANDATE EXTERNAL PROFICIENCY TESTING FOR ER/PR/HER-2 IHC THROUGH THE DIAGNOSTIC ACCREDITATION PROGRAM OF BC
- PROVIDE A LOCALLY GROWN, STATISTICALLY RIGOROUS AND TIMELY TESTING PROGRAM -- BCIPT



TISSUE MICROARRAYS FOR QA

- ASSESSMENT OF INTER-LABORATORY VARIATION IN THE IMMUNOHISTOCHEMICAL DETERMINATION OF ESTROGEN RECEPTOR USING A BREAST CANCER TISSUE ARRAY (Parker et al, AJCP, May 2002)
- MULTIPLE TUMOR TISSUE MICROARRAYS ARE AN EFFECTIVE QUALITY ASSURANCE TOOL FOR DIAGNOSTIC IMMUNOHISTOCHEMISTRY (Hsu et al, Mod Path, Dec 2002)

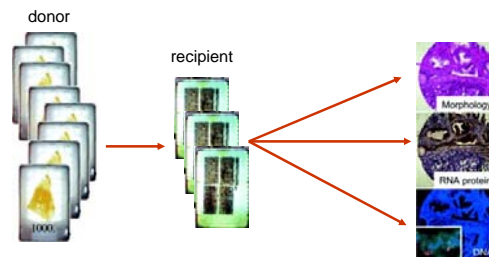


Tissue microarrays ("tissue chips")

- Up to 1000 tissue samples on a microscope slide
- High-throughput in situ analysis of DNA, RNA and protein

Kononen et al. Nat Med. 1998 Jul; 4(7):844-7

Tissue Microarrays





TMA's increase both the efficiency and power of clin-path studies

- Old way: 1000 cases Her 2 FISH study \$1-200,000 (1000 slides to be scored)
- New way: 1000 cases on three slides <\$1,000 (3 slides to be scored)
- Old way: new markers heralded by multiple small studies on different cohorts of patients

Assessment of Inter-laboratory Variability in the Immunohistochemical Determination of Estrogen Receptor Status Using A Breast Cancer Tissue Microarray

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R. Wolber, D. Grant, J.X. O'Connell,
M. Akbari, B. Dupuis & B. Gilks

OBJECTIVES

To assess inter-laboratory and inter-observer variability for the immunohistochemical determination of ER status in invasive breast cancers using tissue microarray technology.

METHODS

Study Population:

- 29 consecutive cases of invasive breast cancer collected at UBC Hospital from April to Dec. 2000
 - > 26 primary tumors, 2 axillary lymph node metastases, and 1 chest wall recurrence
 - > 6 cases ER negative (0 staining) and 23 ER positive (three 1+, ten 2+ and ten 3+ staining)

Distribution Of ER Scores For Each Laboratory Applying The 0 – 3+ Scoring System

ER Score	Lab 1	Lab 2	Lab 3	Lab 4
0	13	13	11	15
1+	7	7	9	13
2+	14	18	20	18
3+	16	16	12	9
N/A*	8	4	6	3

* n/a = number of cores not assessed

Inter-laboratory Comparison Of ER Reporting: Lab 1 vs Lab 2

		Lab 2				Lab 2		
		0	1	2		-ve	+ve	
		3						
Lab 1	0	11	2		Lab 1	11	2	
	1		4	2				
	2		3	13		1		39
	3			5		11		
		K = 0.64				K = 0.88		

Inter-laboratory Comparison Of ER Reporting: Lab 4 vs Lab 1

		Lab 1				Lab 1		
		0	1	2		-ve	+ve	
		3						
Lab 4	0	11	1	1	1	Lab 4	11	3
	1	1	5	7				
	2		1	8	10			39
	3			2	6			
		K = 0.41				K = 0.77		

Inter-laboratory Agreement For ER Reporting Among 5 B.C. Laboratories

- Comparison of 4 labs using the 0 to 3+ scoring system revealed an overall K = 0.54 (range 0.41 to 0.69)
- Comparison of 5 labs interpreting cores as positive vs negative revealed an overall K = 0.84 (range 0.64 to 1.0)
- Lab 4 showed only fair concordance with the other labs

Intra-laboratory Inter-observer Agreement for ER Reporting

- The inter-observer agreement between 5 pathologists within Lab 4 was high:
 - Overall K = 0.76 for 0-3+ scoring
- There was also excellent agreement with an outside observer:
 - K = 0.85 for 0-3+ scoring

CONCLUSIONS

- The breast cancer tissue microarray proved to be an effective and efficient tool for assessing variation in ER reporting among laboratories in B.C.
- Inter-laboratory and inter-observer agreement for the IHC determination of ER status were generally good
- Variability in ER reporting was predominantly due to technical factors

Table 4: Interlaboratory comparison of S-100 staining

		VGH*	A	B	C	D	E
Breast	Carcinoma	(1/18) 5.6%	(2/16) 12.5%	(1/15) 6.7%	(5/14) 35.7%	(2/14) 14.3%	(1/14) 7.1%
Cervix	Carcinoma	(2/29) 6.9%	(0/31) 0%	(1/27) 3.7%	(2/26) 7.7%	(1/26) 3.8%	(1/29) 3.4%
Kidney	Carcinoma	(0/10) 0%	(0/9) 0%	(4/8) 50%	(0/7) 0%	(0/8) 0%	(0/9) 0%
Liver	Carcinoma	(0/5) 0%	(0/5) 0%	(1/5) 20%	(0/5) 0%	(0/5) 0%	(0/5) 0%
Lung	Carcinoma	(0/7) 0%	(0/3) 0%	(0/5) 0%	(0/5) 0%	(0/5) 0%	(0/5) 0%
Pleura	Mesothelioma	(0/10) 0%	(0/10) 0%	(0/10) 0%	(0/10) 0%	(1/10) 10%	(0/10) 0%
Ovary	Carcinoma	(1/11) 9.1%	(1/11) 9.1%	(4/11) 36.4%	(2/13) 15.4%	(0/13) 0%	(2/14) 14.3%
Prostate	Carcinoma	(0/14) 0%	(0/13) 0%	(0/13) 0%	(0/13) 0%	(0/13) 0%	(0/13) 0%
Soft Tissue	Sarcoma	(2/29) 6.9%	(2/29) 6.9%	(3/26) 11.5%	(4/28) 14.3%	(2/29) 6.9%	(4/25) 16%
Testis	Germ Cell	(0/10) 0%	(0/7) 0%	(1/8) 12.5%	(0/7) 0%	(0/7) 0%	(0/7) 0%
Thyroid	Carcinoma	(2/13) 15.4%	(0/10) 0%	(6/10) 60%	(4/10) 40%	(1/10) 10%	(4/10) 40%
Vulva	Carcinoma	(0/6) 0%	(0/4) 0%	(0/2) 0%	(0/2) 0%	(0/2) 0%	(0/3) 0%
Skin	Melanoma	(5/5) 100%	(3/3) 100%	(4/5) 80%	(4/4) 100%	(4/4) 100%	(4/4) 100%

* VGH = Vancouver General Hospital, while A-E are five other diagnostic immunohistochemistry laboratories
 Results are expressed as (number of positive cases/total number of cases) % positive

