Root cause analysis of pre-microscopic errors in anatomical pathology using Eindhoven classification

Fakeha Rehman,[1] Muhammad Saqlain Haider,[2] Rakhshindah Bajwa,[3] Muhammad Raheel Anwar,[4] Muhammad Zeeshan Sarwar,[5] Fatima Naumeri,[6] Zayed Rashid[7]

Abstract

Objective: To evaluate pre-microscopic errors in anatomical pathology.

Methods: The cross-sectional descriptive study was conducted at the Department of Pathology of a tertiary care hospital in Lahore, Pakistan, from September, 2016, to January, 2017, and comprised surgical pathology specimens. Errors were noted across the pre-microscopic process. Defects per million opportunities were calculated to determine sigma metric value in every step, from requisition to slide preparation. Root cause analysis was applied to the process of histology preparation to identify the root cause of each previously identified problem using Eindhoven classification. All errors were recorded on a pre-designed proforma.

Results: There were 2420 specimens. While errors were encountered in all phases of the pre-microscopic process, but the (G6: n=1085, 44.83%), followed by requisition (R3: n=893, 36.9%) and cover slipping (C1: n=776, 32.06%).

Conclusion: Development of standard procedures and protocols with staff training is likely to help in controlling the errors.

Keywords: Anatomical pathology, Eindhoven, Errors, Root cause analysis, six sigma metrics. (JPMA 70: 0000; 2020)
https://doi.org/10.5455/JPMA.5565

Introduction

Errors are an integral part of human actions and healthcare systems. Surgical pathology errors are inevitable during any phase of laboratory testing, including pre-analytical, analytical and post-analytical phases. However, the main challenge is timely identification and rectification of these errors to ensure effective patient safety.[1] Surgical specimen errors can lead to delays in diagnosis and treatment, misdiagnosis, inappropriate treatment, repeat procedures or re-operations, and emotional distress or physical harm. Elimination of these errors is important for correct and valid diagnosis and for the provision of better treatment. Every area of laboratory should evaluate all possible errors and seek measures to avoid such errors.[2]

Many studies have been published[3-5] analysing errors in all phases of routine processing in anatomical pathology with a reported error rate of 35% in specimen labelling.[1] Local data on identification and evaluation of errors in anatomical pathology is scarce, but a study evaluated errors in a high volume clinical chemistry laboratory with an error rate of 0.45% and sigma level of 5.2.[6]

[1,3,4]Department of Pathology, [5]East Surgical Ward, [7]Student, Final Year MBBS, King Edward Medical University, Lahore, [2]Department of Pathology, Tehsil Healthcare Unit, Nankana Sahib, Punjab, [6]Pediatric Surgery Ward, King Edward Medical University, Mayo Hospital, Lahore, Pakistan.
Correspondence: Fakeha Rehman. Email: sohnia@gmail.com

There are no existent well-defined structured tools to measure pre-microscopic errors in anatomical pathology. In addition, Eindhoven classification has not been previously used in our part of the world to identify potential sources in system that lead to these errors.[4]

The current study was planned to evaluate pre-microscopic errors in anatomical pathology using Sigma metric analysis and Eindhoven's classification

Material and Methods

The cross-sectional descriptive study was conducted at the Department of Pathology of a tertiary care hospital in Lahore, Pakistan, from September, 2016, to January, 2017, and comprised surgical biopsy specimens.

After obtaining approval from the institutional review board (IRB), the sample size was calculated with 95% confidence level, 5% margin of error and expected error percentage 7.6%.[1] Data was collected from all the surgical biopsy specimens submitted to the department using non-probability convenience sampling. Specimens submitted for frozen section and cytological analysis were excluded.

The study used pre-existing tissue obtained for clinical purposes from human subjects, and, thus, it was deemed to carry "minimal risk," and the requirement for informed consent was waived by the IRB. The questionnaire exploring the errors was prepared after extensive literature search.[1-3,5,7-11] It included the type of error

Table-1: Types of errors with error codes.

Stage in Process	Error code	Error Category
Requisition	R1	No specimen in container
	R2	Mislabelled specimen
	R3	Incomplete requisition
Accession	A1	Inappropriate container
	A2	Pathology number allocation error
	A3	Inappropriate fixative volume ratio
	A4	Autolysed specimen
Grossing	G1	Incorrect orientation
	G2	Cross contamination
	G3	Mislabelled cassette
	G4	Inappropriate cassette selection
	G5	Inappropriate ink application
	G6	Inappropriate selection of tissue section
	G7	Staples in specimen
	G8	Sectioning with Blunt blade
	G9	Thick sections
	G10	Inappropriate Decalcification
Fixation	F1	Inappropriate fixative
	F2	Inappropriate fixative pH
	F3	Insufficient fixation time
Processing	P1	Inappropriate processing schedule
	P2	Inappropriate reagent concentration
	P3	Inappropriate heat/vacuum/agitation
	P4	Non-compatible reagents
	P5	Inadequate reagent exposure
	P6	Loss of specimen
Embedding	E1	Uneven tissue
	E2	Froth artifact
	E3	Extra tissue outside of cassette
	E4	Inappropriate mold selection
	E5	Improper orientation
	E6	Tissue damage due to excessive heat
Slide drying	D1	Improper slide drainage before drying
	D2	Inadequate drying temperature
	D3	Inadequate drying time
Staining	S1	Staining too light
	S2	Staining too heavy
	S3	Uneven staining
	S4	Stain contamination (inadequate filtration)
	S5	Loss of stain contrast between nuclear & cytoplasmic stain
	S6	Weak or faded cytoplasmic stain (Eosin)
	S7	Nuclei blurry or smudgy appearance
	S8	Inappropriate pH
Cover slipping	C1	Air bubble
	C2	Cover slip scratched
	C3	Section cloudy

observed in each phase, date on which the error was observed, and the person who observed the error. The questionnaire was later distributed among faculty members and subject specialists for content validity. Technical staff was distributed at each station accordingly. Error rate was analysed in all the pre-microscopic processes, including requisition, grossing, fixation, processing, embedding, microtomy, staining and cover slipping. The types of errors were noted and coded in the first step (Table-1). Six Sigma is a metric that quantifies the performance of processes as a rate of Defects per Million Opportunities (DPMO).[3,6-8] Six Sigma programmes also encompass robust techniques such as Define-Measure-Analyse-Improve-Control (DMAIC) and Root Cause Analysis (RCA) to find and eliminate defects and variation within a process (Figure-1). DPMO is defined as the average number of defects per unit divided by the number of opportunities to make a defect on the product during that run normalised to one million. Opportunity is the lowest defect noticeable by the customer.

Table-2: Reference table for six sigma metrics calculation.

Six Sigma Metrics Value	DPMO
1	690,000
2	308,000
3	66,800
4	6,210
5	320
6	3.4

DPMO: Defects-Per-Million Opportunities.

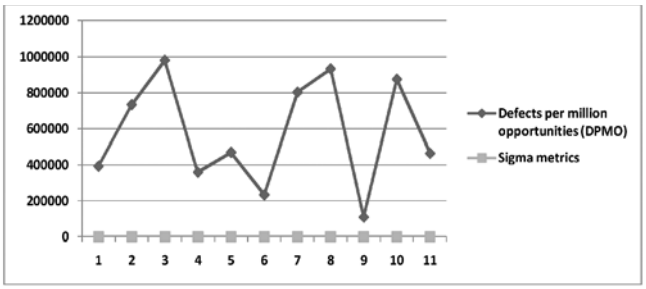

Figure-1: Relationship between defects per million opportunities (DPMO) and six sigma metrics.

In order to calculate DPMO, three distinct pieces of information are required: the number of units (tests) produced; the number of defect opportunities per unit (test); and the number of defects.[8,12]

$$DPMO = \frac{\text{Number of Defects X } 1{,}000{,}000}{(\text{Number of Defect Opportunities/Unit}) \times \text{Number of Units})}$$

Using the Six Sigma metrics reference table (Table-2), DPMOs and Sigma metrics for errors every step of the specimen processing were calculated.[6-8]

RCA was applied to the process of histology preparation in order to identify the root cause of each previously identified problem using Eindhoven classification.[4]

Results

There were 2420 samples. Errors were reported in all stages of the surgical specimen handling process, with the highest frequency in grossing (G6: n=1085, 44.83%) (Figure-3), followed by requisition (R3: n=893, 36.9%) and cover slipping (C1: n=776, 32.06%) (Table-3). RCA done using Eindhoven classification revealed contributing factors, like lack of organisation, inappropriate process flow, poor knowledge and unawareness of facts regarding patient safety (Table-4, 5).

Table-3: Error coding, percentage with DPMOand six sigma metrics calculation.

Stage in Process	Error code	Error Category	No. of Errors	% of errors (n=2420)	DPMO	Sigma metrics
Requisition	R1	No specimen in container	05	0.2	2066	4.4
	R2	Mislabelled specimen	54	2.23	22314	3.6
	R3	Incomplete requisition	893	36.9	369008	1.9
Accession	A1	Inappropriate container	689	28.47	284711	2.1
	A2	Pathology number allocation error	68	2.8	28099	3.5
	A3	Inappropriate fixative volume ratio	783	32.35	323554	2.0
	A4	Autolysed specimen	234	9.66	96694	2.9
Grossing	G1	Incorrect orientation	337	13.92	139256	2.6
	G2	Cross contamination	429	17.72	177273	2.5
	G3	Mislabelled cassette	192	7.93	79339	3.0
	G4	Inappropriate cassette selection	69	2.85	28512	3.5
	G5	Inappropriate ink application	665	27.47	274793	2.1
	G6	Inappropriate selection of tissue section	1085	44.83	448347	1.7
	G7	Staples in specimen	0	0	0	--
	G8	Sectioning with Blunt blade	185	7.64	76446	3.0
	G9	Thick sections	243	10.04	100413	2.8
	G10	Inappropriate Decalcification	86	3.55	35537	3.4
Fixation	F1	Inappropriate fixative	205	8.47	84711	2.9
	F2	Inappropriate fixative pH	167	6.9	69008	3.0
	F3	Insufficient fixation time	498	20.57	205785	2.4
	P1	Inappropriate processing schedule	582	24.04	240496	2.3
Processing	P2	Inappropriate reagent concentration	145	5.99	59917	3.1
	P3	Inappropriate heat/vacuum/agitation	108	4.46	44628	3.2
	P4	Non-compatible reagents	178	7.35	73554	3.0
	P5	Inadequate reagent exposure	32	1.32	13223	3.8
	P6	Loss of specimen	92	3.8	38017	3.3
	E1	Uneven tissue	120	4.95	49587	3.2
Embedding	E2	Froth artifact	89	3.67	36777	3.3
	E3	Extra tissue outside of cassette	61	2.52	25207	3.5
	E4	Inappropriate mold selection	87	3.59	35950	3.3
	E5	Improper orientation	154	6.36	63636	3.1
	E6	Tissue damage due to excessive heat	56	2.31	23140	3.5
	M1	Knife lines (Dull blade)	52	2.14	21488	3.6
Microtomy	M2	Cracked/torn section (block too cold)	141	5.82	58264	3.1
	M3	Inappropriate Ribbon thickness	363	15	150000	2.6
	M4	Chattering (speedily cutting of blocks)	83	3.42	34298	3.4
	M5	Folds	472	19.5	195041	2.4
	M6	Uneven spacing	112	4.62	46281	3.2
	M7	Compression artifact (improper knife tilt angle)	232	9.58	95868	2.9
	M8	Slide mislabelled/number not legible	467	19.29	192975	2.4
	M9	Block exhaustion	21	0.86	8678	3.9
	FL1	Un-cleaned slides	630	26.03	260331	2.2
Flotation	FL2	Cross contamination	225	9.27	92975	2.9
	FL3	Wrinkles in section	158	14	65289	3.1
	FL4	Bubbles	190	7.85	78512	3.0
	FL5	Section lifting (adhesive not used)	12	0.49	4959	4.1

Contd. on next page >>>

	FL6	Inappropriate ribbon selection	367	15.16	151653	2.6
	FL7	Ribbon damage during lifting	149	6.15	61570	3.1
	FL8	Un-cleaned water	186	7.68	76860	3.0
Slide drying	D1	Improper slide drainage before drying	34	1.4	14050	3.7
	D2	Inadequate drying temperature	180	7.43	74380	3.0
	D3	Inadequate drying time	53	2.19	21901	3.6
Staining	S1	Staining too light	291	12.02	120248	2.7
	S2	Staining too heavy	65	2.68	26860	3.5
	S3	Uneven staining	685	28.3	283058	2.1
	S4	Stain contamination (inadequate filtration)	70	2.89	28926	3.4
	S5	Loss of stain contrast between nuclear & cytoplasmic stain	387	15.99	159917	2.5
	S6	Weak or faded cytoplasmic stain (Eosin)	284	11.73	117355	2.7
	S7	Nuclei blurry or smudgy appearance	336	13.88	138843	2.6
	S8	Inappropriate pH	187	7.72	77273	3.0
Cover slipping	C1	Air bubble	776	32.06	320661	2.0
	C2	Cover slip scratched	36	1.48	14876	3.7
	C3	Section cloudy	313	12.93	129339	2.7

DPMO: Defects-Per-Million Opportunities.

Table-4: Eindhoven classification model for latent root causes in surgical pathology.

Category	Description	Code
LATENT ERRORS	**Errors That Result From Underlying System Failures**	
Technical	Physical items such as equipment, physical installations, software, materials, labels, and forms	
External	Failures beyond organization's control & responsibility	TEX
Design	Failure due to poor design of equipment, form, software, labels.	TD
Construction	Construction failure despite correct design	
	Laboratory construction does not allow a one-by-one flow of specimens, No space constructed for specimen setup	TC
Material	Material defects classified not under TC or TD	
	Defects in grossing examination utensils, specimen bags, specimen containers, printed labels, etc.	TM
Organisational		
External	Failures at an organizational level beyond organization's control & responsibility	OEX
Protocols and procedures	*Protocols and procedures are too complicated, inaccurate, unrealistic, absent, or poorly presented.*	OP
Transfer of knowledge	*Inadequate measures taken to ensure that situational or site-specific knowledge or information of accessioning, specimen setup, and biopsy gross examination, processing etc. is transferred to all new staff. Inability to transfer patient safety practices and methods of learning.*	OK
Management priorities	*Upper level management decisions in which patient and worker safety is relegated to an inferior position when there are conflicting demands or objectives. Conflict between production needs and patient safety.*	OM
Culture	*The laboratory culture not safety oriented and fear driven. Unprofessional behaviours tolerated at all system levels.*	OC
ACTIVE ERRORS (HUMAN)	**Errors or failure resulting from human behavior**	
External	Human failures originating beyond the control & responsibility of organization	HEX
Knowledge based behaviours		HKK
Knowledge-based errors	Inability of an individual to apply existing knowledge to a novel situation	
Rule based behaviours		
Qualification	Incorrect fit between individual's qualification, training or education and a particular task	HRQ
Coordination	Lack of task coordination within a healthcare team in an organization	HRC
Verification	Failure in correct & complete assessment of the situation, including relevant condition of the patient	HRV
Intervention	Faulty task planning & execution (selecting wrong protocol or carrying out right protocol in wrong way)	HRI
Monitoring	Failure in process monitoring	HRM
Skill-based behaviours		
Slips	Failures in performance of fine motor skills	HSS
Tripping	Failures in whole body movement	HST
OTHERS		
Patient related	Failures related to patient characteristics that are beyond staff control	PRF
Unclassifiable	Failures that cannot be classified in any other category	X

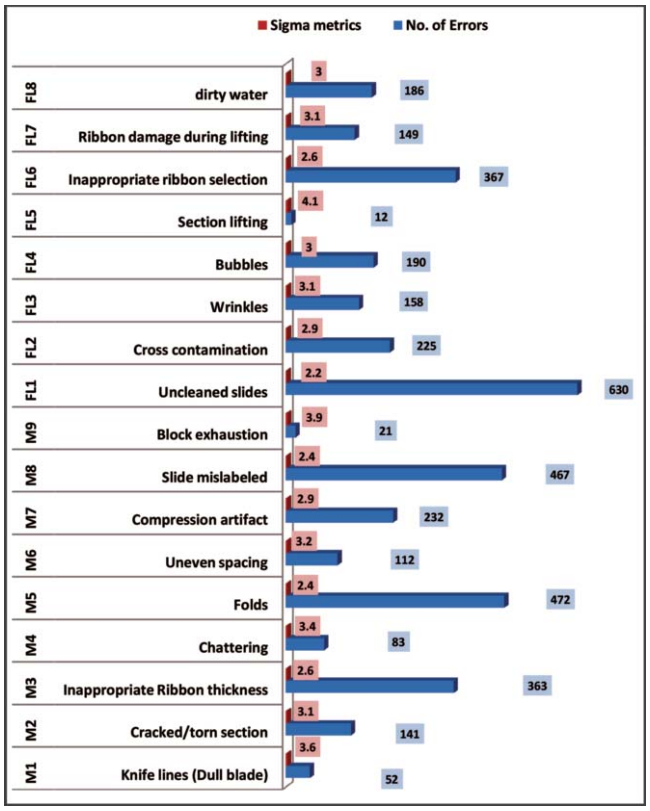

Figure-2: Microtomy and floatation errors with six sigma metrics value.

Discussion

Histopathological diagnosis of tissue sections is wholly dependent upon microscopic examination and interpretation. Basic requirements for arriving at a conclusive diagnosis include correct biopsy procedure, proper fixation and processing techniques, adequate sectioning and staining. RCA is an effective way to highlight errors in routine histopathology and their attributes. Six Sigma is a technique that allows objective assessment of process performance. Several studies have examined the importance of Sigma metrics in quantifying the performance of an analytical testing process.[7-11] In our study, Six Sigma metrics value for all the steps involved in the production of slides specimen receiving and processing was less than 3 which is far less than previously reported;[1,4-6] indicating lack of quality management and standard protocols.

Majority of requisition errors (36%, Sigma metrics 1.9) were due to insufficient clinical information needed for specimen processing and histological diagnosis which was in contrast to 3.6% and 6% reported earlier.[1,13] A study revealed that additional clinical information resulted in amended reports in 10% cases.[14,15] Second major requisition and accessioning error was mainly due to the use of inappropriate container and inadequate fixative volume ratio. There was no technical staff assigned for the accessioning bench. Maximum errors were noted in grossing, floatation of tissue sections and

Table-5: Assessment of Eindhoven classification model latent root causes in pre-microscopic specimen handling.

Stage in Process	Error Category	Root cause analysis using Eindhoven classification
Requisition	R1	
	R2	OE, OK
	R3	
Accession	A1	
	A2	
	A3	OP, HKK, OE, OC, OK, TC
	A4	
Grossing	G1	
	G2	
	G3	
	G4	
	G5	HKK, HRI, OC, TD,
	G6	OK, HRV, HRI, OK,
	G7	HRC, TM, HRM
	G8	
	G9	
	G10	
Fixation	F1	
	F2	HKK, HRM, HRC
	F3	
Processing	P1	
	P2	
	P3	HKK, TM, TEX
	P4	HKM, TD, HRM
	P5	OC
	P6	
Embedding	E1	
	E2	
	E3	HRM, HRI, HKK, HRM, HRQ, OC, OK
	E4	
	E5	
	E6	
Slide drying	D1	
	D2	HKK, HRI, HKM
	D3	
Staining	S1	
	S2	
	S3	
	S4	HKK, HKM, HRI, TM
	S5	
	S6	
	S7	
	S8	
Cover slipping	C1	
	C2	TM
	C3	

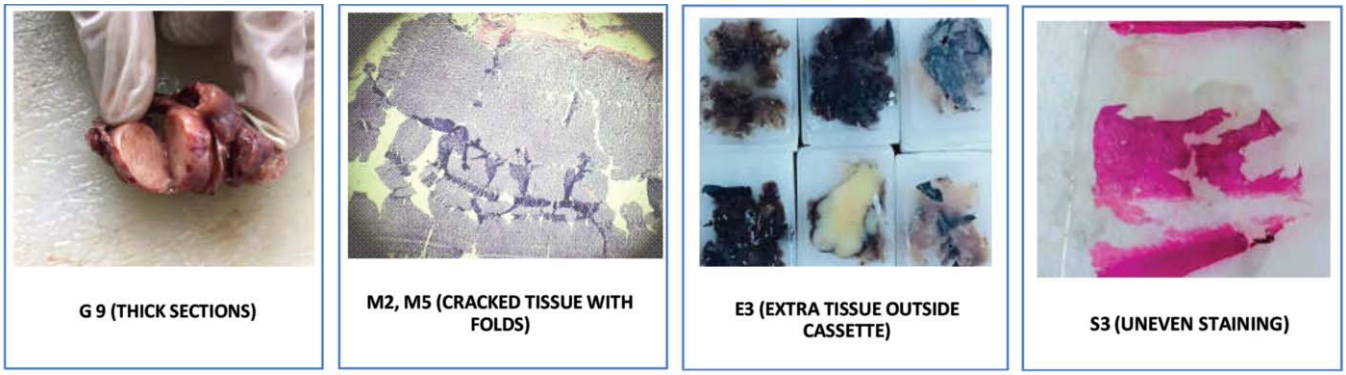

Figure-3: Different types of pre-microscopic errors.

routine H&E staining. In one study, errors detected in each phase were: accessioning (6.5%), gross dissecting (28%), processing (1.5%), embedding (4.5%), tissue cutting and slide mounting (23%), staining, (1.5%), labelling and releasing (35%)[1] (Figure-3).

Grossing errors were attributed to lack of knowledge, training and expertise in resident pathologists. Study carried out in Brazil revealed that inappropriate macroscopic description of the specimen and inadequate representative sections may result in a very serious damage to the patient.[15] A study proposed a patient safety curriculum for anatomical pathology residents to improve their skills and, in turn, provision of improved patient care.[16] A study at a Nigerian laboratory observed that majority of errors were due to missing demographic information on request forms (22.8%), poor technical quality of slide sections (18.4%) and typographical errors by the typists (12.3%).[17]

Processing errors were mainly due to running wrong processing schedules (24%, Sigma metrics 2.3) occurring as a result of inconsistency in the level of knowledge and training of different technicians handling the equipment. Improper tissue orientation (6%, Sigma metrics 3.1) during embedding may result in missing the relevant diagnostic material. Inappropriate ribbon thickness (15%, Sigma metrics 2.6), tissue folds, mislabelled slides were the major causative factors, resulting in microtomy errors (Figures-2, 3). Floaters and carry-overs may result in near-missed events, thus affecting final histological diagnosis as demonstrated in a study.[18,19] Most of the artefacts during staining are due to altered staining intensity as a result of low-quality stains, impurities attributed to insufficient filtration of staining solutions, and lack of potential of hydrogen (pH) and temperature monitoring[17,19] (Figure-3). Majority of technicians never consulted equipment manual for handling operating errors; whereas the technical persons of the relevant companies supplying the equipment lacked the sufficient knowledge and competency to handle trouble-shootings. Standard operating procedures (SOPs) were either lacking or were not being followed (Table-5).

According to a study, the higher the number of methods with a Sigma metric of 5 or better, the lower are the costs for reagents, supplies and control material required to monitor the performance of the methods.[8] RCA in the current study revealed that most of the pre-microscopic errors were due to failure in workflow process, inappropriate knowledge and malpractice of laboratory workers, provision of low-quality reagents, lack of organisational standards and responsibilities (Table-5).

The unwillingness of laboratory workers to report errors, lack of laboratory information system for data retrieval, improper record maintenance and data entry on registers and charts, and lack of organisational support were limitations of the current study.

Findings of the current study indicate that by highlighting the most relevant points of interest, it is possible to improve both the methodology and the procedural safety. A follow-up study is recommended after the adoption of lean methodology to re-evaluate the impact of new quality measures on Six Sigma metrics. Furthermore, errors in the post-analytical phase and other tests, including fine needle aspiration cytology (FNAC) and frozen sections, should also be subjected to Six Sigma metrics and RCA using Eindhoven classification.

Conclusion

Errors were found at almost every step of the process. A step-wise implementation of quality control and strict internal audit are needed to avoid these errors which significantly affect test results and customer satisfaction, thus sabotaging the laboratory image.

Disclaimer: None.

Conflict of Interest: The person who signed the ethical review statement was also a co-author.

Source of Funding: None.

References

1. Morelli P, Porazzi E, Ruspini M, Restelli U, Banfi G. Analysis of errors in histology by root cause analysis: a pilot study. J Prev Med Hyg. 2013; 54:90-6.
2. Steelman VM, Williams TL, Szekendi MK, Halverson AL, Dintzis SM, Pavkovic S. Surgical Specimen Management: A Descriptive Study of 648 Adverse Events and Near Misses. Arch Pathol Lab Med. 2016; 140: 1390-6.
3. Smith ML, Raab SS. Assessment of latent factors contributing to error: addressing surgical pathology error wisely. Arch Pathol Lab Med. 2011; 135: 1436-40.
4. Schaaf TWV. Near-miss reporting in the chemical process industry; an overview. Microelectron Reliab. 1995; 35:1233-43.
5. Nakhleh RE, Idowu MO, Souers RJ, Meier FA, Bekeris LG. Mislabelling of cases, specimens, blocks, and slides: A College of American Pathologists study of 136 institutions. Arch Pathol Lab Med. 2011; 135: 969-74.
6. Jafri L, Khan AH, Ghani F, Shakeel S, Raheem A, Siddiqui I. Error identification in a high volume clinical chemistry laboratory: Five-year experience. Scand J Clin Invest. 2015; 75: 296-300.
7. Meier FA. The landscape of error in surgical pathology. In: Nakhleh RE, eds. Error reduction and preventions in surgical pathology. New York: Springer, 2015; pp 3-26.
8. Litten J. Applying six sigma metrics to reduce outliers. Clin Lab Med. 2017; 37: 177-86.
9. Brown RW. Quality management in the laboratory. In: Nakhleh RE, Fitzgibbons PL, eds. Quality management in anatomic pathology: promoting patient safety through systems improvement and error reduction. North field, Illinois: college of American Pathologists, 2005; 77-92.
10. Rolls G. 101 steps to better histology. Leica Microsystems education series. [Online] [Cited 2018 August 18]. Available from: URL: https://leicabiosystem.com/pathologyleaders/101-steps-to-better-histology-a-practical-guide-to-good-histology-practice.
11. Michael CW, Naik K, Zhou M, Zhang Y, Gong W, Mohamed SO, et al. Value Stream Mapping of the Pap Test Processing Procedure; A Lean Approach to Improve Quality and Efficiency. Am J Clin Pathol. 2013; 139: 574-83.
12. Westguard S. Prioritizing risk analysis quality control plans based on sigma metrics. Clin Lab Med. 2013; 33: 41-53.
13. Nakhleh RE. Error reduction and prevention in surgical pathology. Arch Pathol Lab Med. 2008; 132:181-5.
14. Nakhleh RE, Zarbo RJ. Amended reports in surgical pathology and implications for diagnostic error detection and avoidance: a College of American Pathologists' Q-Probes study of 1 667 547 accessioned cases in 359 laboratories. Arch Pathol Lab Med. 1998; 22:303-9.
15. Sanatana MF, Ferreira LCL. Diagnostic errors in surgical pathology. J Bras Pathol Med Lab. 2017; 53: 124-29.
16. Samulski TD, Mantone K, Livolsi V, Patel K, Baloch Z. Patient safety curriculum for anatomical pathology trainees: recommendations based on institutional experiences. Adv Anat Pathol. 2016; 23:112-7.
17. Malami SA, Iliyasu Y. Local audit of diagnostic surgical pathology as a tool for quality assurance. Niger J Med. 2008; 17:186-90.
18. Platt E, Sommer P, McDonald L, Bennett A, Hunt J. Tissue floaters and contaminants in the histology laboratory. Arch Pathol Lab Med. 2009; 133: 973-8.
19. Rastogi V, Puri N, Arora S, Kaur G, Yada L, Sharma R. Artefacts: A diagnostic dilemma review. J Clin Diagn Res. 2013; 7: 2408-13.