Mastering AVI

Part 5: Transition from Manual to automated visual Inspection

- Interpretation of inspection results and validation data
- Considerations on validation program for automated inspection
- Performance measurement
- Maintaining the manual inspection

PDA Parenteral Drug Association

Instructor Lead: Romain Veillon / Fernand Koert / Sébastien Koch

CONNECTING PEOPLE SCIENCE AND REGULATION®

MVI remains Golden Standard

Some method comparison but MVI is the golden standard

Automated Visual Inspection (AVI)

- ✓ High speed and high capability
- ✓ Highly reproducible
- ✓ Consistent (no fatigue effect)
- ✓ Defects presentation

- ✓ High initial investment
- ✓ Works within strict condition (validated upstream process)
- ✓ Detect “only” preset defects
- ✓ Indiscriminative (i.e.: fiber and cracks are seen the same way)
- ✓ Some uncovered area
- ✓ Higher false reject rate

Semi-Automated Visual Inspection (SAVI)

- ✓ Adaptation
- ✓ Speed
- ✓ Brain
- ✓ Flexible
- ✓ Decision capable

- ✓ Inconsistent (fatigue effect)
- ✓ Not highly reproducible
- ✓ Susceptible to influence
- ✓ Some uncovered area
- ✓ Monotonous repeated work
- ✓ Significant training effort

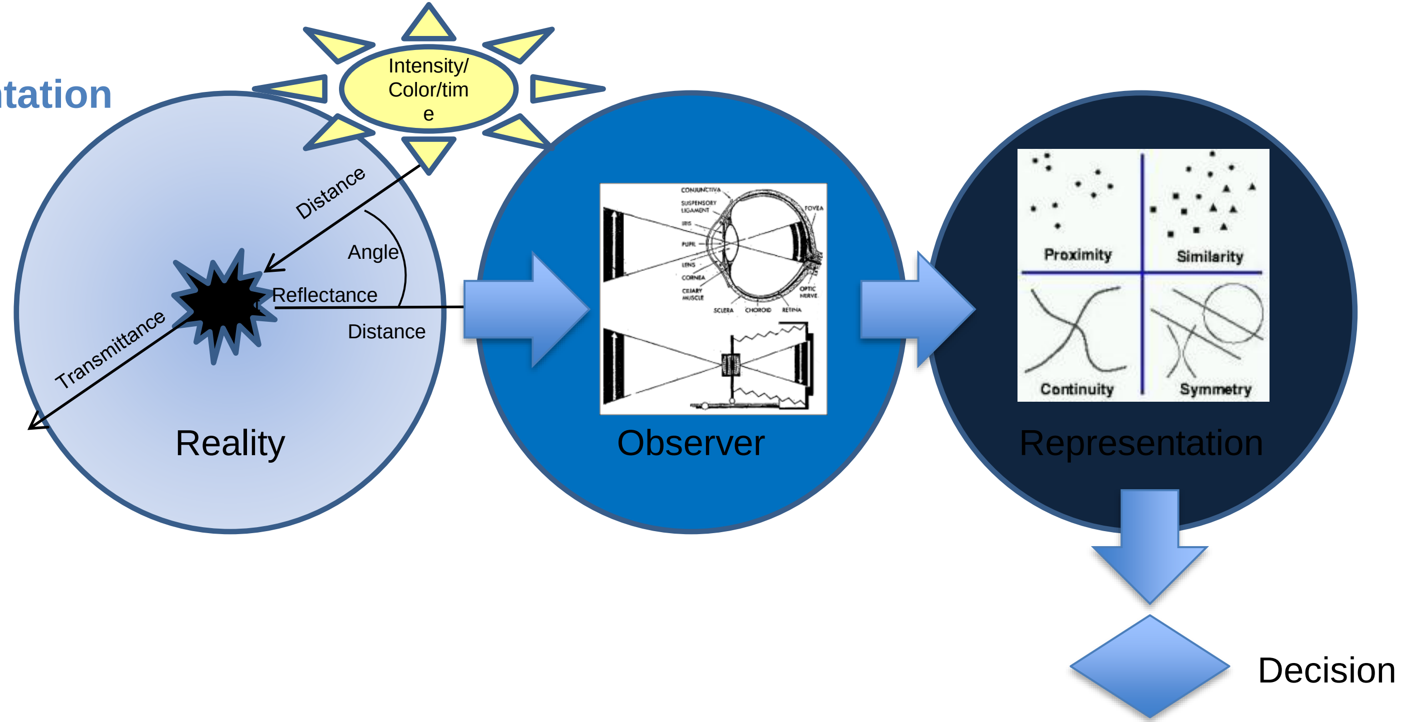
Manual Visual Inspection (MVI)

- ✓ Adaptation
- ✓ Brain
- ✓ Flexible
- ✓ Decision capable
- ✓ Classification of defects

- ✓ Inconsistent (fatigue effect, emotional)
- ✓ Not highly reproducible
- ✓ Susceptible to influence
- ✓ Slow
- ✓ Monotonous repeated work

Inspection steps from object presentation to decision

Object presentation



Example of MVI interpretation with color continuity : SNOW can be blue ?

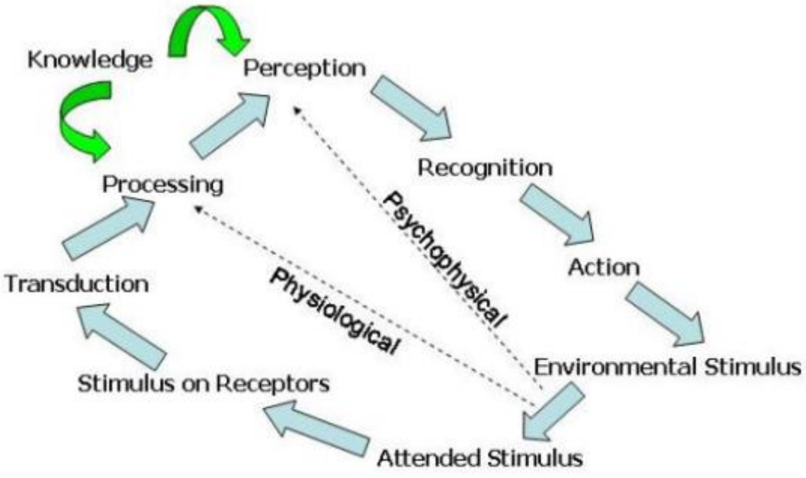
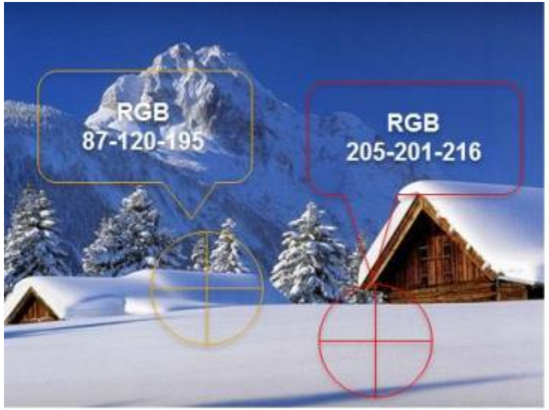
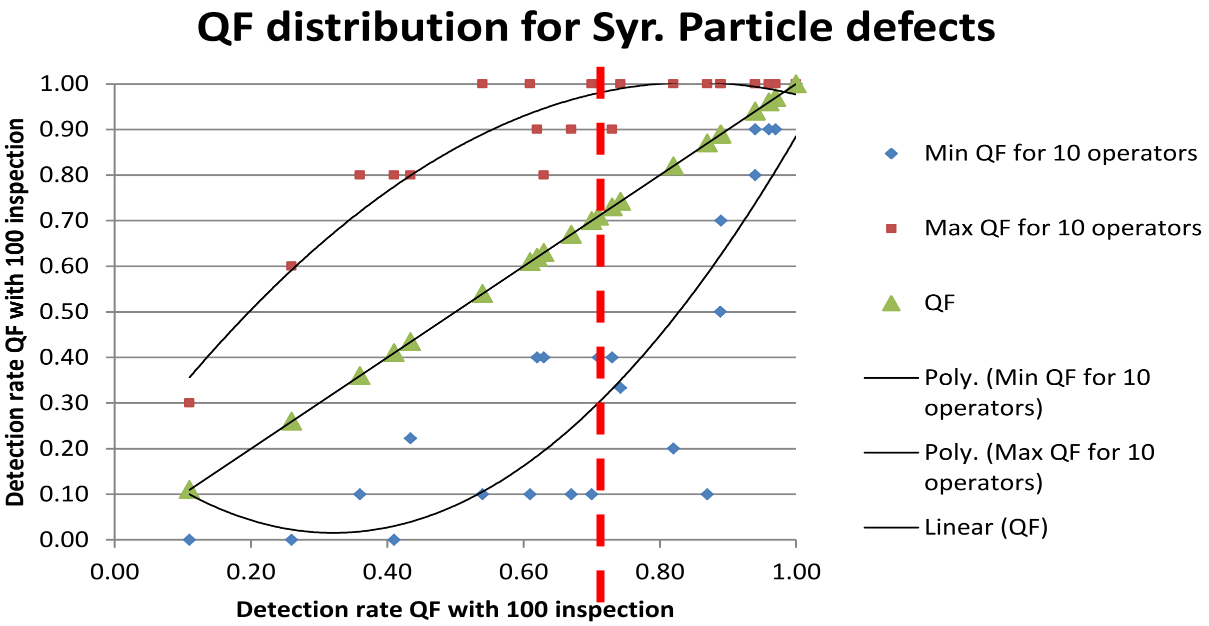


Figure 1.1: The Perceptual Process



Chromatic continuity:
We see snow even when color changes drastically (RGB)

MVI inter-operator variability increases with smaller defects



Key learning:
Particle detection in MVI is highly probabilistic: operator variability is lower with very high QF > 0.70
Operator variability higher with lower QF [0.3:0.8]
To compare AVI to MVI need to be in true defect zone where inter-operator variability is lower

Vision Recipe development

Computer Vision recipe Development Principle

- Defect kits

Defect kit + Good units

- GBs Image

Images on machine

- Set up vision

Vision Recipe set up

- Data model

Data archive & modeled

- ppk

Statistic Capability

Iterative loop if test failed

- Limits

limit critical parameter

- Go
- No Go

Evaluation

Key learning: vision development should be done by vision engineers with some statistical background
To start during machine development with supplier

Establish MVI baseline

Manual Visual inspection Baseline study (Knapp)

Particle defect

Defect type . . . Defect type

Glass defect

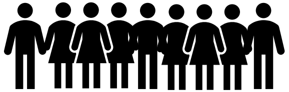
Defect type . . . Defect type

Closure defect

Defect type . . . Defect type

Other ..defect

. . .



10 operators

1 standard work MVI

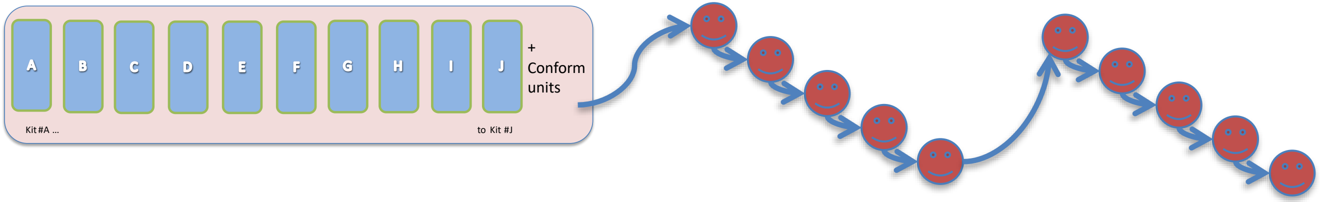
Average Probability of
detection (PoD)
for each defect type

Example of standard MVI Baseline evaluation

Key learning:
Proposal for methology for MVI baseline evaluation

Material and Methods

- [10 kits + good units] = 1 inspection lot order
- No information given to inspectors = routine inspection
- No interactions with inspectors to avoid any interferences
- Changed shift to avoid interactions between inspectors
- 1 inspection every day during 2/3 weeks, one inspector at a time
- Kit verified every day for defect state, replaced broken units to identical
- QF Result compiled for each inspector



Example of standard MVI Baseline evaluation

Material and Methods

Data reporting: QF = number of ejected / number of inspected

	Operators	1	2	3	4	5	6	7	8	9	10
KIT	**DEFECT**										
Kit A	Defect #1										
Kit A	Defect #...										
Kit A	Defect #nn										
……….	…………										
Kit J	Defect #1										
Kit J	Defect #...										
Kit J	Defect #nn	QF1	…..		…….			QF10			

QF #1A

………..

QF #nn

QF #1J

………..

QF #nn

MRZE

Key learning:

Rigorous Baseline evaluation of MVI performance is key to succeed AVI validations
Mind Data integrity control
Good documentation practices

Kapp Digested

Julius Knapp : Deterministic ≠ probabilistic

Since the particulate visibility statement in the XIX Revision of the Pharmacopeia (9) is based upon a deterministic human inspection it is inappropriate and should be discarded.

With both manual and automated systems regarded as probabilistic, they can now be similarly evaluated and their demonstrated capability rigorously compared.

longevity estimates. The particular containers rejected in any single inspection cannot be accurately predicted except for two special cases: those containers that are absolutely clean and are never rejected and those containers with gross defects that are rejected in every inspection.

Key learning:
MVI and AVI remain probabilistic by nature

Uhlir pioneer work for method comparison: Venn diagram

In terms of the two-dimensional probabilistic inspection model, Uhlir utilized two unrelated one-dimensional probability distributions: manual and machine. In consequence, the differing sensitivities of the two methods can yield the Venn diagram result shown in Figure 1. Here, the manual inspection and the automated device perform in exemplary fashion. Figure 1 indicates, however, that the sets of containers rejected by each method had few containers in common. This comparison suggests that the Uhlir evaluation methodology may not generate the demonstration of equivalence that CGMP's require in the validation of alternative inspection methodologies and devices.

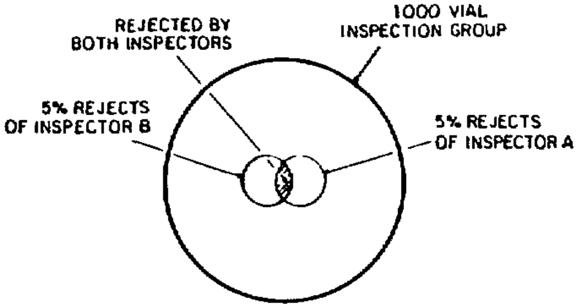


Figure 1—Venn diagram of two inspector particulate inspection demonstrating the expected paradoxial results.

Key learning:

Between multiple operators in MVI there is no contingency, meaning even if they have similar performance they cannot not detect same defects

Why Correlogram unit by units does not make sense ?

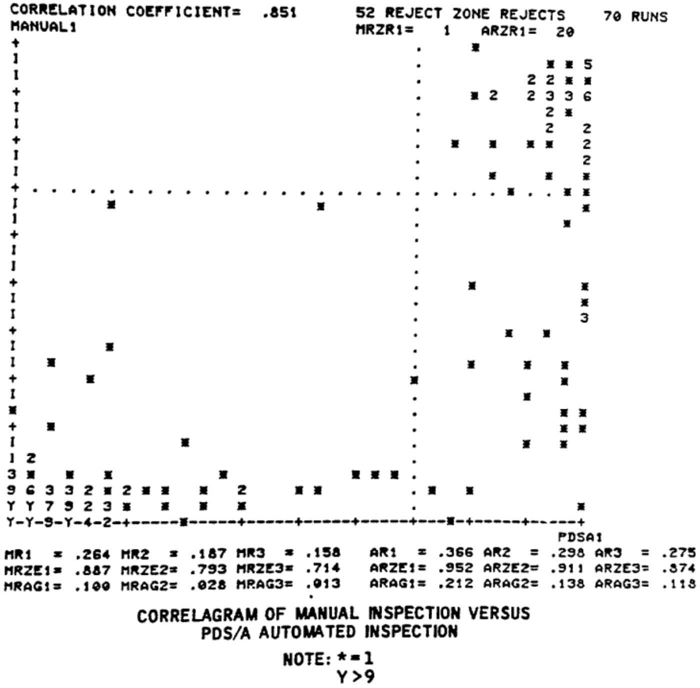


Figure 3—Correlagram comparing the results of 72 manual and 70 PDA/A inspections. A comparison summary of the two inspection methods is included in the computer printout. Of major interest is the fact that only 1 (MRZR1) of the 52 were rejected manually with a probability of 1.0. The PDA/A rejected 20 (ARZR1) of the 52 with a probability of 1.0. The plusses on each axis are the 10% increment points from a rejection probability of 0 to 1.0. The abscissa is for the automated system; the manual system rejection probability is the ordinate. The dotted lines shown are the Reject Zone boundaries for both systems. The * symbols indicate a single container at a point in the plane, a Y indicates a number of containers greater than 9. Values between 2 and 9 are shown directly. The reject rate, R, the Reject Zone Efficiency, RZE, and the undesired reject rate in the Accept and Gray Zones, RAG, are tabulated under the histogram with suffix 1, 2, and 3 to indicate sequential inspection number. The prefix N indicates manual inspection; the A prefix indicates an automatic inspection.

Key take Away:

When J Knapp draw a correlogram of between 2 method, each plot is the number of units in each probability class

That is NOT paired comparison per DEFECT

The capability of one process relative to the other cannot be evaluated until the correlation between the results of both inspections is established. This correlation is based on an examination of the inspection history of each container in each inspection process. Sufficient inspection replications are required to assure statistically reproducible results with acceptable tolerance intervals. Since we are dealing with probabilistically defined quantities, statistical tools must be used. The basic questions of replicability, relative per-

Classification of defects by « iso-probability subgroup »

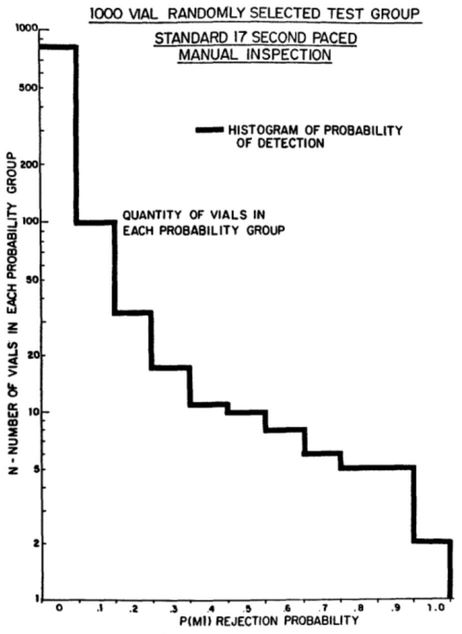


Figure 2—Histogram of probability of detection for a 1000 vial randomly selected test group. The Schering standard 17 second paced manual inspection was employed.

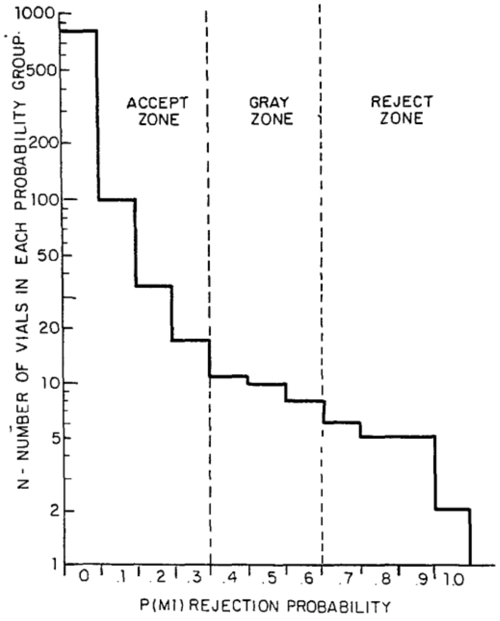


Figure A2—One-dimensional histogram of a normal batch showing the accept Gray and Reject Zones defined by the human based standard inspection.

PDA
Parenteral Drug Association

How to compare 2 distribution of probability?

To accomplish this evaluation, two random distributions must be compared.

When the implications of the two dimensional probability plane of Figure A2 are examined it becomes apparent that each entry in either system can be transformed into a distribution in the other system.

TABLE AII. Probabalistic Distribution of Rejection Probabilities for Containers in "Manual" Inspection and "System" I and II

	N(0)	N(.1)	N(.2)	N(.3)	N(.4)	N(.5)	N(.6)	N(.7)	N(.8)	N(.9)	(N1.0)
'MANUAL'	1	1	1	1	1	1	1	1	1	1	1
'SYSTEM' I & II	2.5	1.5	1.5	.5	0	0	0	.5	.5	1.5	2.5

RZEM terminology

$$RZE(M1) = \frac{RZR(M1)}{RZN} = \frac{14.7}{18} = 81.7\%$$

(Eq. 4)

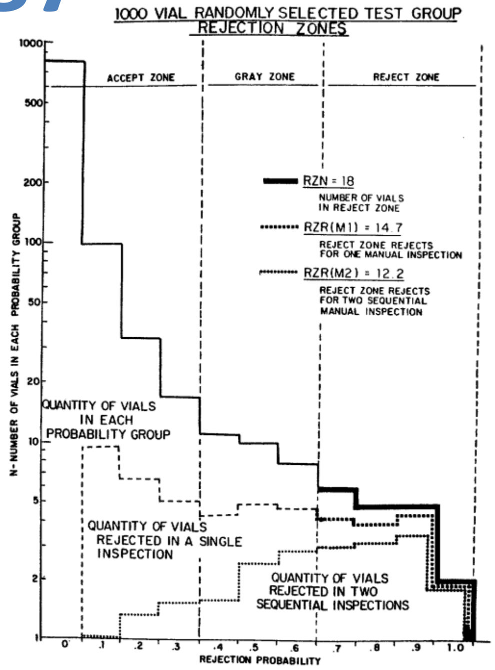
RZE(Mn) = efficiency of rejection in Reject Zone

RZN(Mn) = number of vials identified in the manual Reject Zone

RZR(Mn) = Reject Zone reject quantity as defined in manual inspection

$$RZE(M2) = \frac{RZR(M2)}{RZN} = \frac{12.2}{18} = 67.7\%$$

RZE = Reject zone efficiency

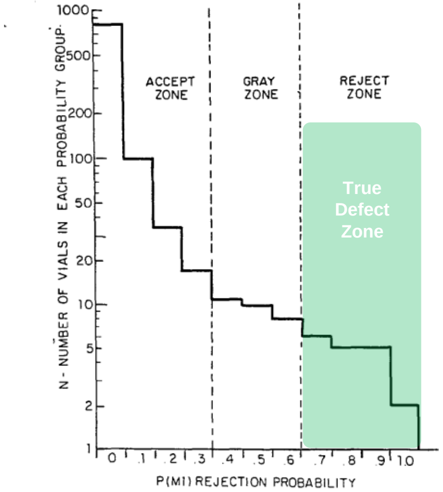


Key take Away:
Now USP has simplified terminology speaking of PoD Probability of Detection

Comparison AVI to MVI

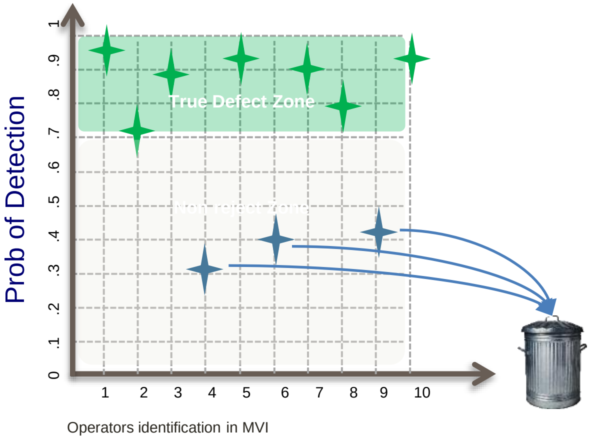
Knapp concept of true defect zone

- ❑Performance of a new method (MVI – SAVI – AVI) must be compared to MVI Baseline PoD established with standard work conditions
- ❑Only defects in the true defect zone are retained, when PoD is above 70%
- ❑Comparison is not a paired comparison defect by defect but rather based on average comparison for a defect family (number of vials in each probability group)

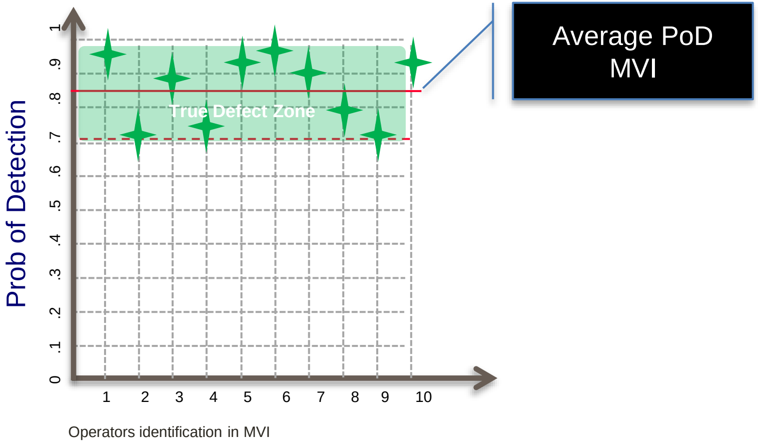


True Defect Zone concept (USP<1790> Knapp)

MVI Baseline performance study by defect family

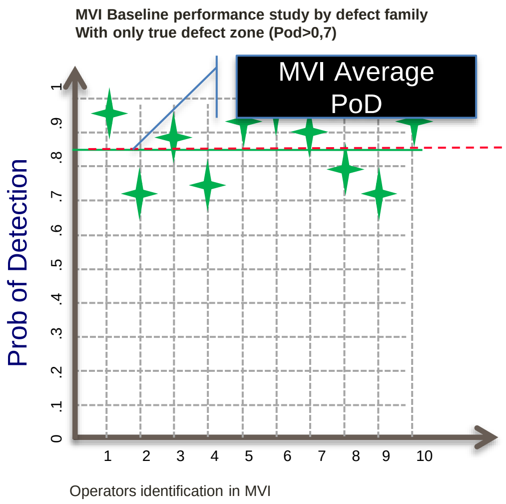


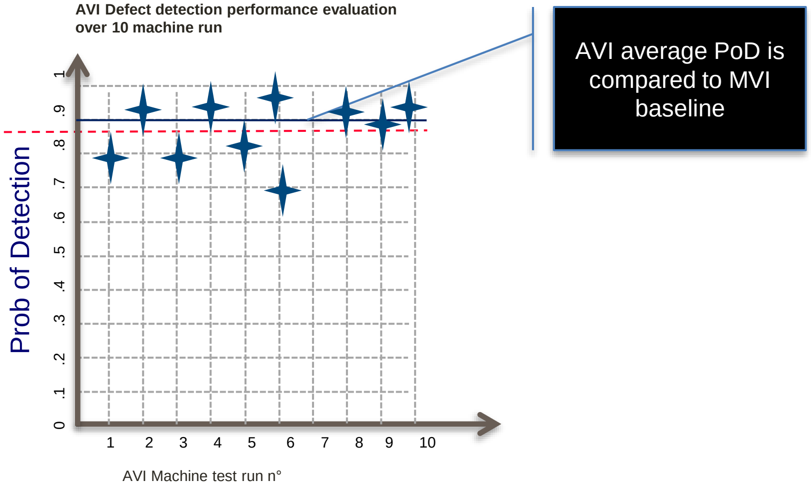
MVI Baseline performance study by defect family
With only true defect zone (Pod>0,7)



Comparison AVI to MVI

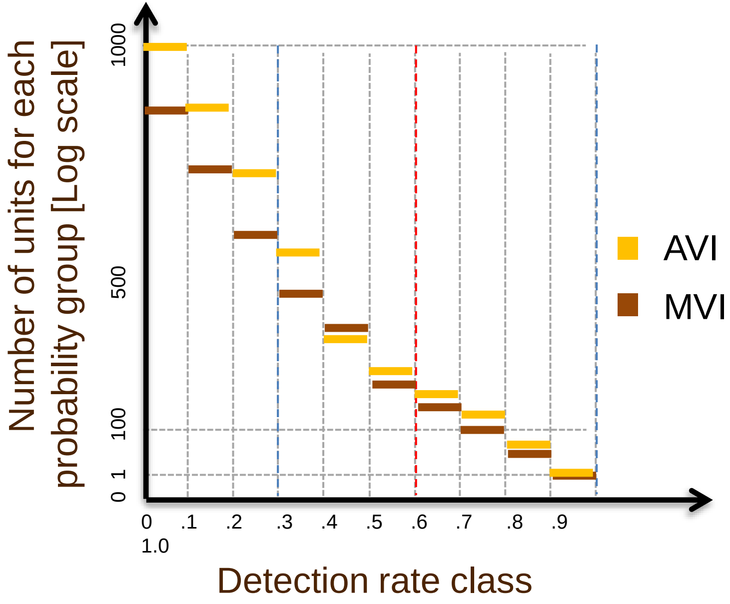
"The capability of one process relative to the other cannot be evaluated until a correlation between the results of both inspections is established. This correlation is based on an examination of the inspection history of each container in each inspection process. Sufficient inspection replications are required to assure statistically reproducible results with acceptable tolerance intervals. Since we are dealing with probabilistically defined quantities, statistical tools must be used." J. Knapp



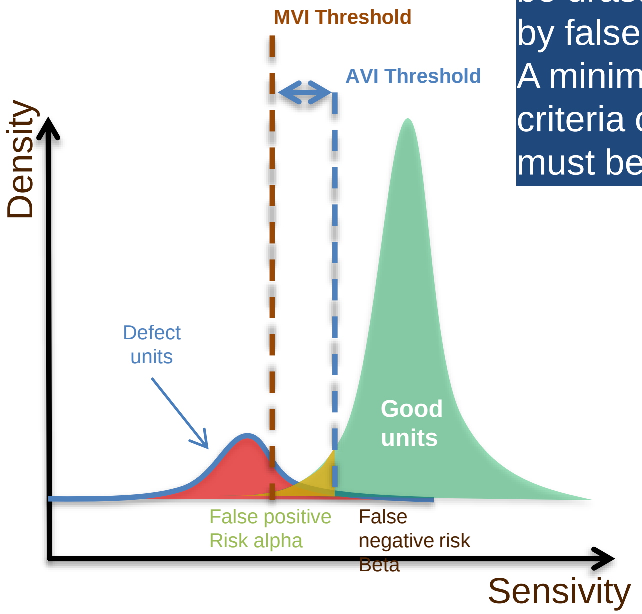


Some Parameters for PQ Design

Why it is critical to control false reject?



=> Comparison of 2 distributions of number of unit having same detection rate

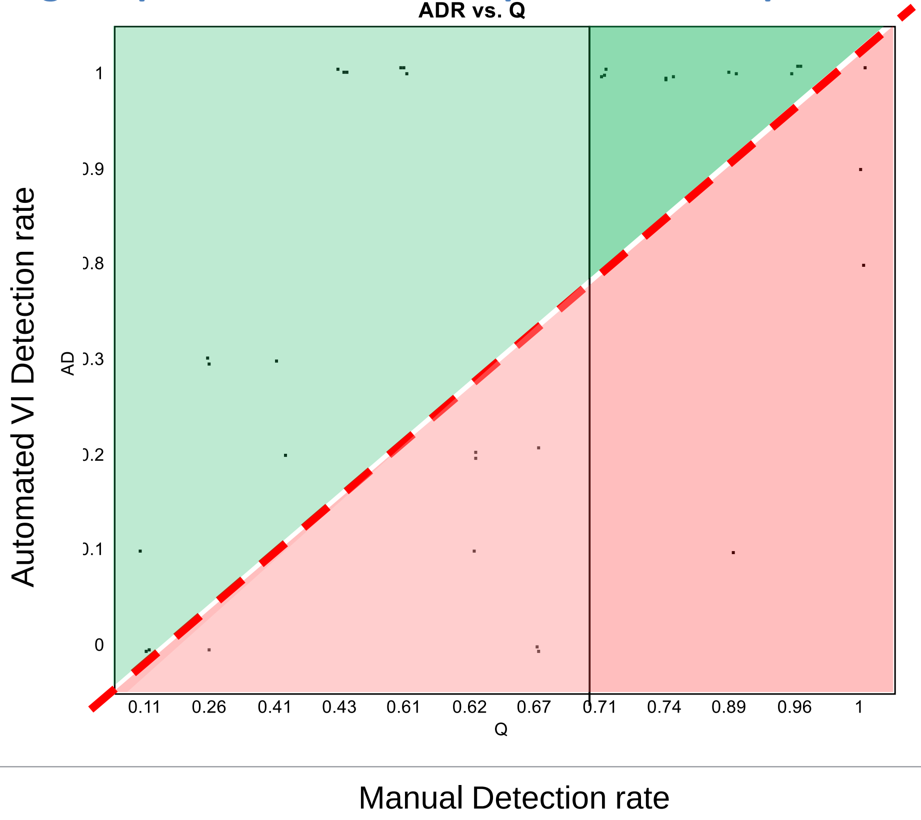


Key take Away:

PoD of defect should not be drastically increased by false reject.

A minimum validity criteria of false reject must be established

Going deeper with a statistical p value to compare AVI vs MVI



Key learning:

Particle detection in AVI has a higher ADR and is less probabilistic than MVI
Specially in range of QF > 0.70

In range with Lower QF
ADR is higher than MVI but more heterogeneity between particles (floating/precipitating)

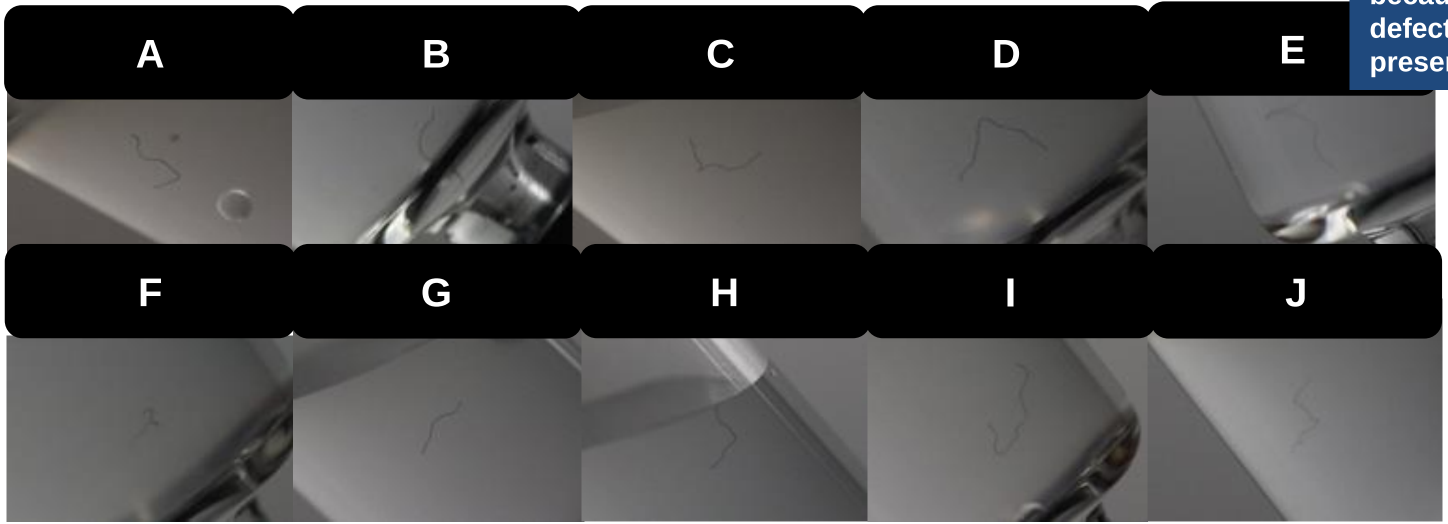
Knapp demonstrated that Validation comparison AVI to MVI should be done in True Defect Zone using "gross defects"

Some individual defect may be lower in detection on some run, the average probability of defect for a defect type (ie particle) must be considered rather than individual paired comparison defect by defect.

Replicate

"The availability of an adequate number of vials in each rejection probability set will be seen to be a prerequisite for successful validation experiments." J.Knapp

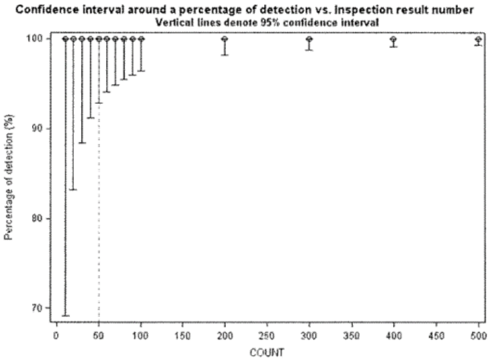
Key learning: At least 3 replicates per defect type should be considered for validation because variability of defect + defect presentation



Impact of number of validation run

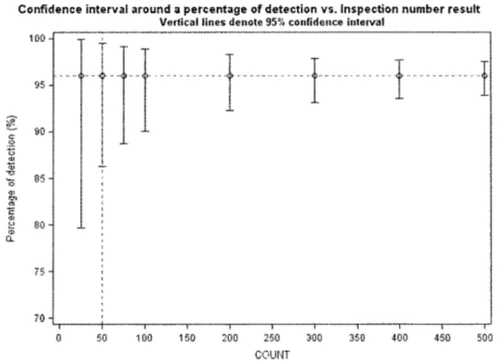
Sample size: practical impact in test run design

With Detection rate limit 100%



With hypothesis of binomial distributions
With 50 runs in validation the confidence interval at 95% is: [92.9% ; 100%]

With Detection rate limit 96%

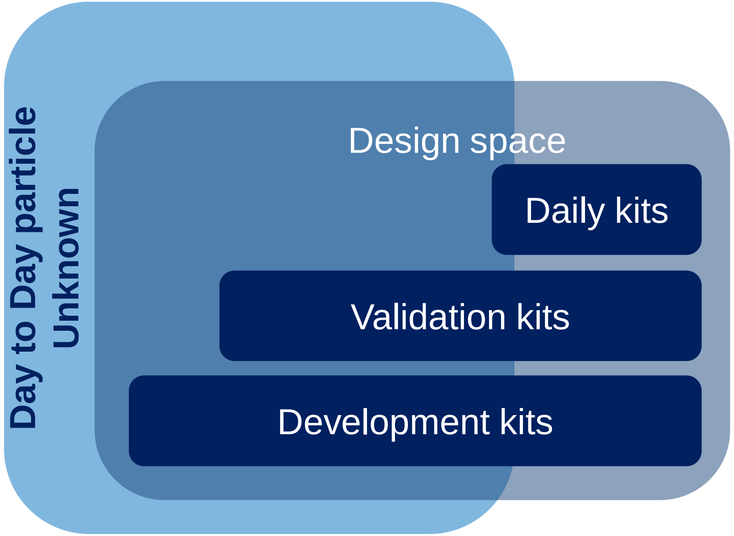


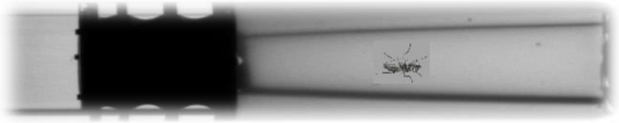
With hypothesis of binomial distributions
With 50 runs in validation the confidence interval at 95% is: [83.6% ; 99.5%]

Key learning: even in case of non probabilistic detection rate criterias, the result remains in a Conf. Int. that depends of number of validation runs

Ability for unknown defects

- Machine vision is designed with minimum threshold, may be compared to high jump.
- Machine vision is designed to detect defects that are outside the design space to anticipate some new defects (unknown)
- With artificial image library we can demonstrate capability of unknown detection (I.e extrinsic)





!example = Fake image!

Key take away:

- In this section you have learnt:

AVI vs MVI	Machine qualification
	Interpretation of inspection results and validation data : Knapp review
	Considerations on validation program for automated inspection
	Performance measurement
	Maintaining the manual inspection