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Expert Elicitation to Populate Early Health Economic Models of Medical Diagnostic Device Development

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Introduction

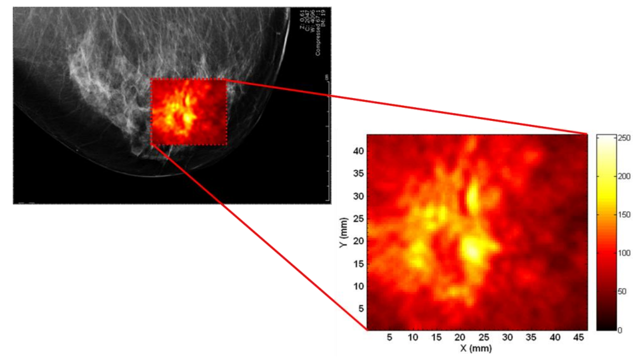
There is an increasing interest to estimate the potential clinical value and likely cost-effectiveness of diagnostic and therapeutic technologies during early development stages to guide further developments. [1,2] Yet, early stages of development are typically characterized by large uncertainty and populating health-economic models with empirical data is not always feasible due to limited availability of data. Elicitation of expert opinions is viewed as an appropriate alternative and may serve as the input for early health economic models. [3]

Figure 1 Flowchart of product development [1]

Objective

In the present study we explore whether expert elicitation is a valid approach to characterize uncertainty regarding the diagnostics performance of photoacoustic imaging in breast cancer. As PAM is still in the translation stage (figure 1) and the prototype is still in development, there is no clinical information available.

Figure 2 Photoacoustic image of breast (Joser, 2009)



By using laser evoked ultrasound waves it is possible to identify vascularization in tissue, as tumor growth is often associated with enhanced blood vessel supply. An important application of this technology includes breast cancer visualization (photoacoustic mammography, PAM).

Methods

Different methods have been applied to evaluate medical technologies in early stages of development e.g. Analytic Hierarchy Process (AHP) [4], and expert elicitation. Expert elicitation is intended to link an expression of an experts' beliefs into a statistical format and has been used a lot in Bayesian statistics because of the need to formulate priors.

We have chosen to use expert elicitation as a method to formulate the knowledge and beliefs of experts about the future performance of PAM and to quantify this information into probability distributions.

Table 1 Expert elicitation

Who is an expert?	
Behavior	Mathematical
What to elicit ?	
Credible interval	Variable vs fixed
Presenting experts' beliefs	Probability Distribution Function vs Cumulative Distribution Function

Sample of experts

Twenty radiologists, specialized in the examination of MR images of breasts, from both academic and non academic hospitals in the Netherlands, were invited to participate in this study as experts.

Calibration method

The purpose of calibration is to receive a relative weighting index for each expert. The weight of each individual expert was determined based on clinical background.

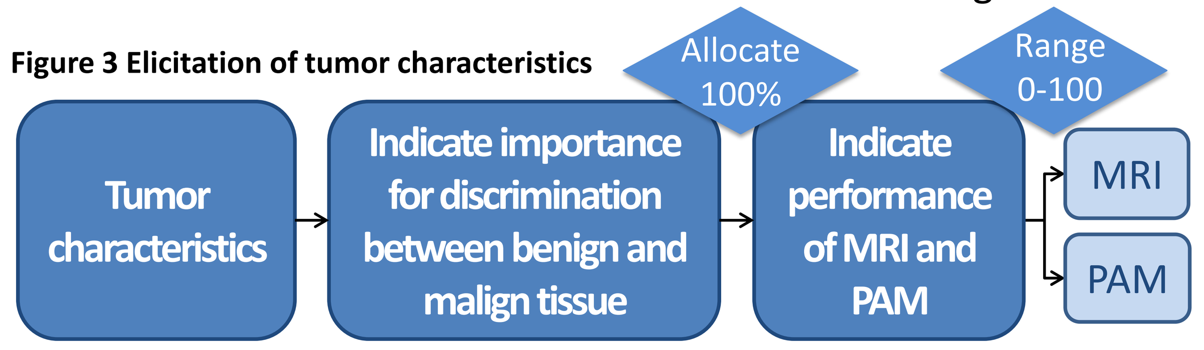
Table 2 Calibration factors

Years of experience (weight 0.45)		Average number of MRI's examined per week (weight 0.45)		Examining MRI's in other areas (weight 0.1)	
X<3	1	X<5	1	X=0	1
X≥3	2	5≤X<10	2	X>0	2
		10≤X	3		

Rating of tumor characteristics

Radiologists are asked to indicate the performance of PAM and MRI for different tumor characteristics used in the examination of images of breasts.

Figure 3 Elicitation of tumor characteristics

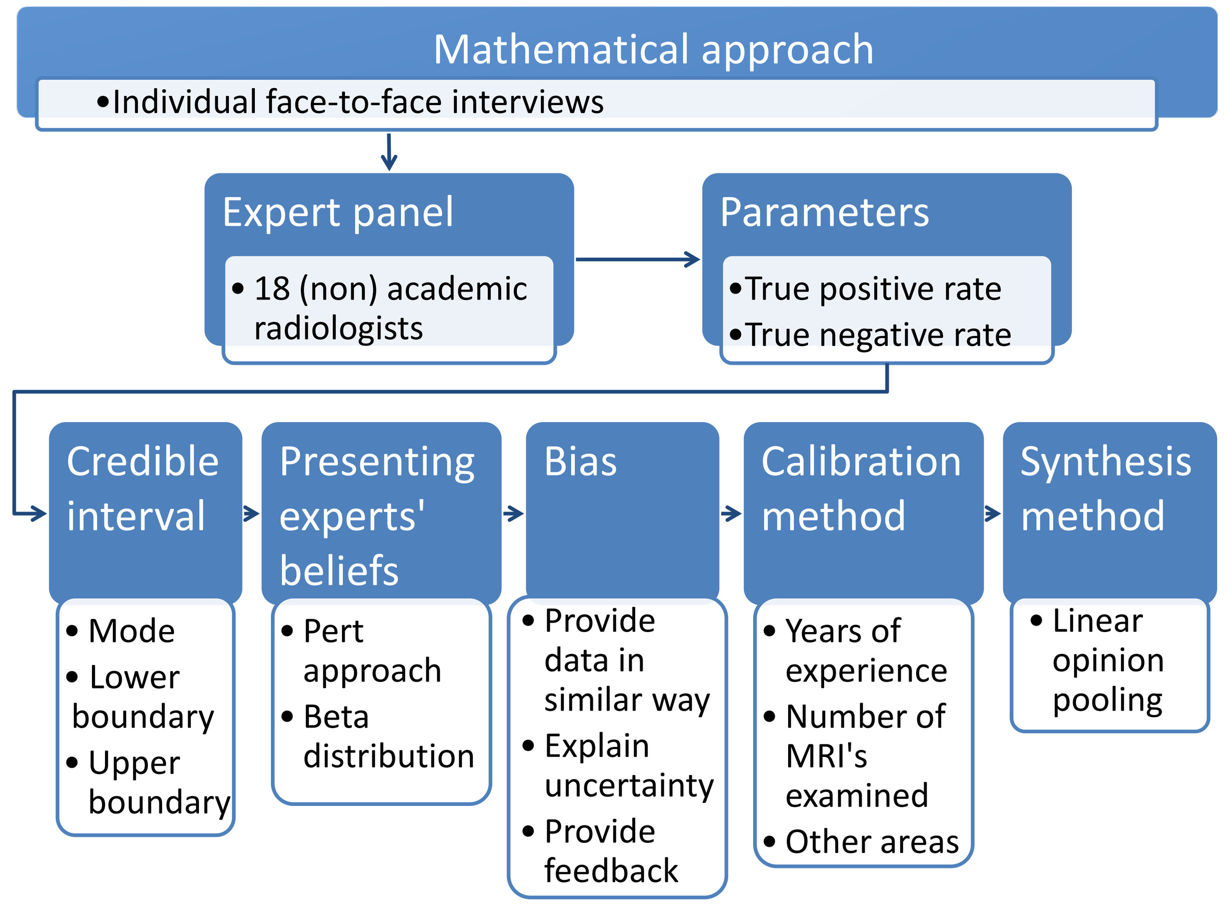


Tumor characteristics are: (1) mass margins, (2) mass shape, (3) mass size, (4) vascularization, (5) localization, (6) oxygen saturation and (7) mechanical properties

Eliciting distributions

A spreadsheet-based (Excel) exercise was designed to elicit the TPR and TNR. Experts received a face-to-face interview of 30 to 45 minutes in which the similar data regarding PAM was presented to each individual radiologist.

Figure 4 Elicitation procedure



Pooled data of MRI was provided based on four studies where MRI was used in a diagnostic setting. For this a 2*2 table was used, where it is sufficient to estimate the TPR and TNR as the false positive rate (FPR), and false negative rate (FNR), will follow from that.

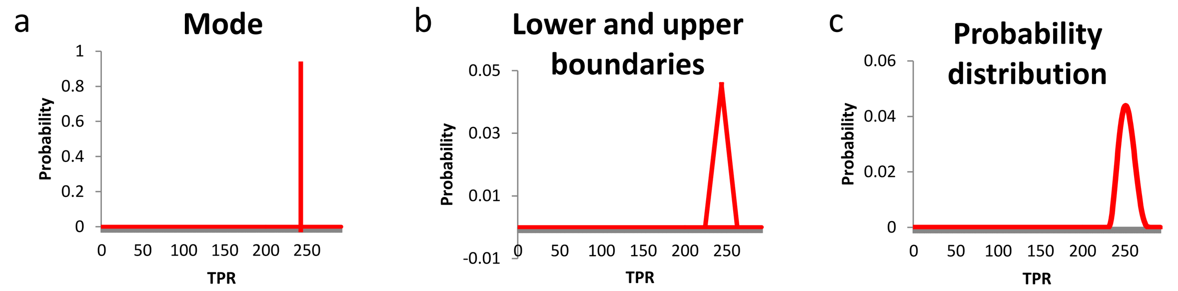
Table 3 Pooled MRI data

	Disease			
Test		Yes	No	Total
	Positive	263	94	357
	Negative	29	214	243
	Total	292	308	600

Probability distribution

Experts were asked to indicate the mode (figure 5a) the lower and the upper boundaries (figure 5b) within a 95% credible interval. With the PERT approach the mean (μ), standard deviation (σ), alpha (α) and beta (β) can be obtained of which the probability distribution (figure 5c) can be determined.

Figure 5 Obtaining probability distribution



Eliciting the mode, than the upper and lower boundaries and by using the PERT approach a probability distribution was obtained.

$$1)\quad \mu = \frac{min + 4 * mode + max}{6} \qquad 2)\quad \beta = \left(\frac{max - \mu}{\mu - min}\right) * \alpha$$

$$3)\quad \sigma = \frac{max - min}{6} \qquad 4)\quad \alpha = \left(\frac{\mu - min}{max - min}\right) * \left(\frac{\mu - min * (max - \mu)}{\sigma^2}\right)$$

$$5)\quad p(\theta) = \sum_{i=1}^{n} w_i p_i(\theta)$$

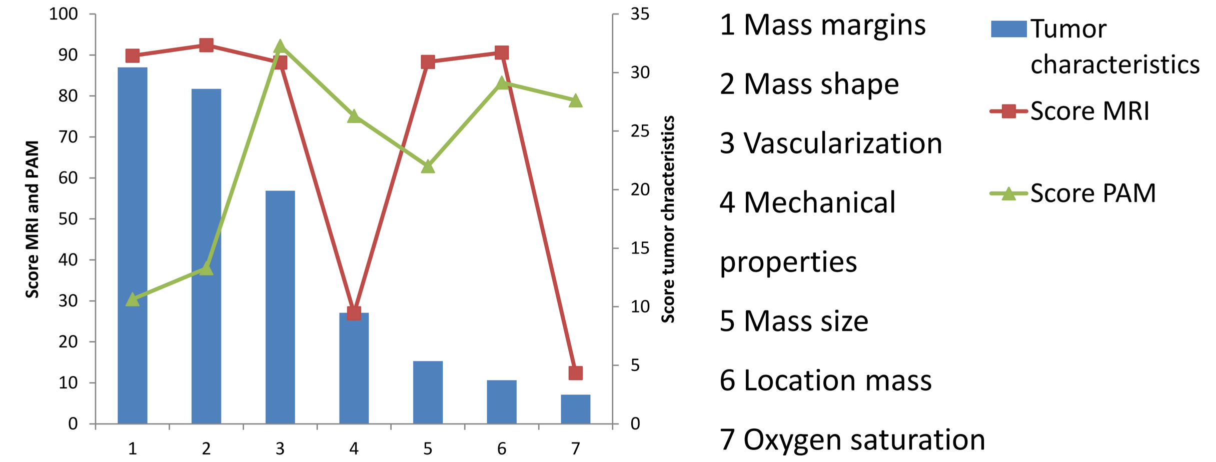
Linear opinion pooling was used to obtain an overall probability distribution, where $p(\Theta)$ is the probability distribution for the unknown parameter Θ and where w_i is the radiologists' i's weight summing up to 1.

Results

Of the 20 radiologists, two radiologists were unable to attend. One radiologist was excluded due to his lack of compliance with the method.

Rating tumor characteristics

Figure 6 Importance tumor characteristics and performance MRI and PAM



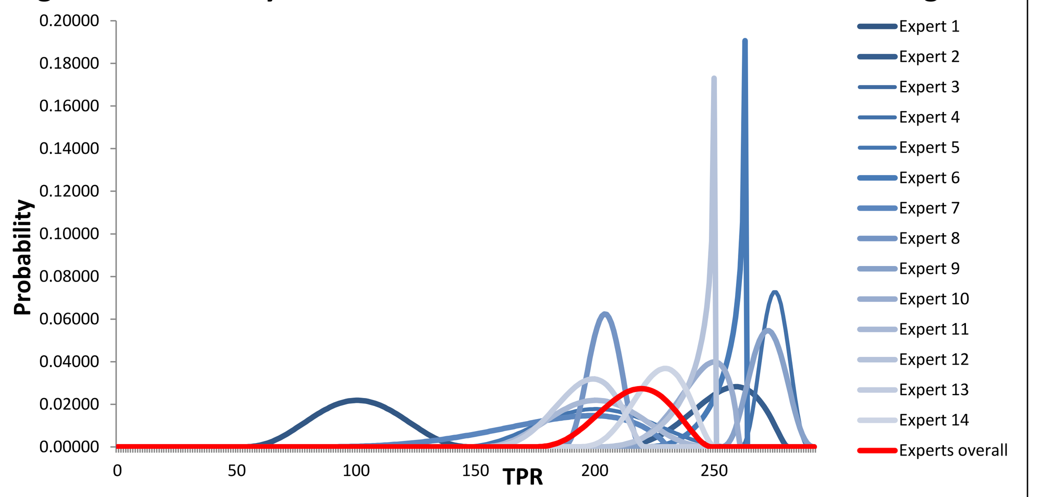
Radiologists indicated that they did not have sufficient data about the added value of oxygen saturation and the mechanical properties.

Sensitivity and specificity

Three out of seventeen radiologists indicated that it was too early to make these estimations due to the absence of data from clinical trials.

Figure 7 shows that there is considerably heterogeneity between radiologists.

Figure 7 Probability distribution of estimations of TPR of 14 radiologists



The sensitivity ranged from 58.9% to 85.1% with a mode of 75.6%. The specificity ranged from 52.2% to 77.6% with a mode of 66.5%.

Conclusion

- Experts estimated the mode of the sensitivity and specificity of PAM to be 75.6% and 66.5%, which is lower than MRI (90.1% and 69.5%).
- Experts expressed difficulties estimating the performance of PAM based on limited data regarding PAM.
- To improve the validity of radiologists' estimations in this study, it is desirable to elicit priors for specific tumor types, since radiologists indicated to base their estimations on an aggregate expectation about how PAM will visualize the various tumor types.
- Further clinical trials should be commissioned to indicate whether these results are valid and expert elicitation could be used in early technology assessment. Before that, the use of the elicited priors in health economic models requires careful consideration.

References

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