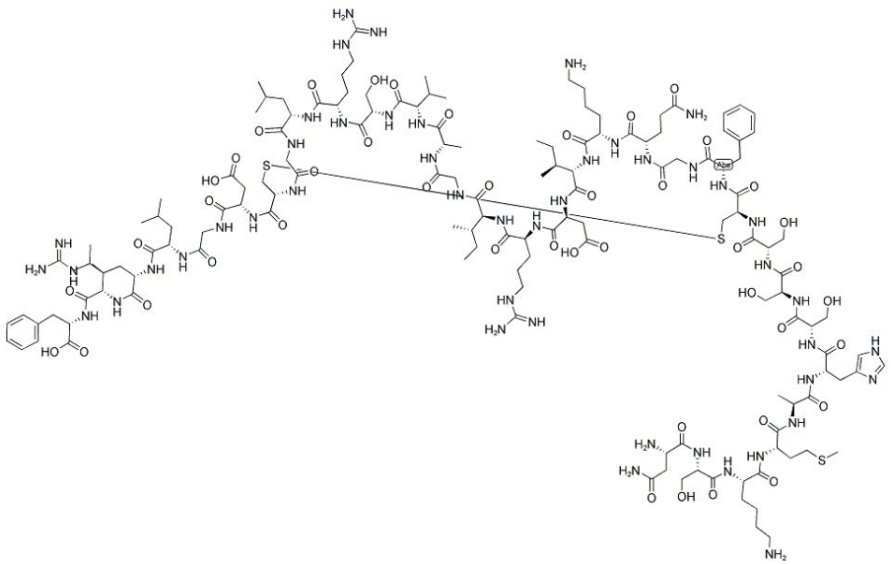
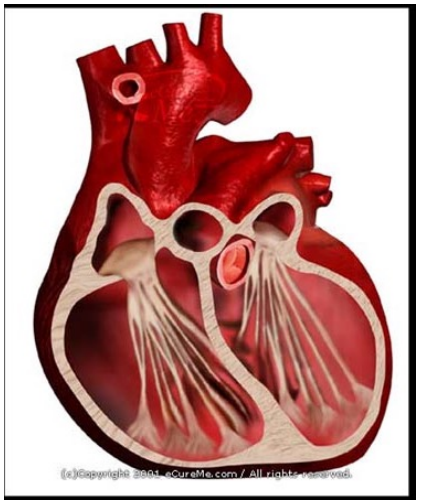




BNP & NTPro-BNP

Comparison of the diagnostic accuracy of BNP & NTPro-BNP in Acute and Chronic Heart Failure

by Jamie Al-Nasir

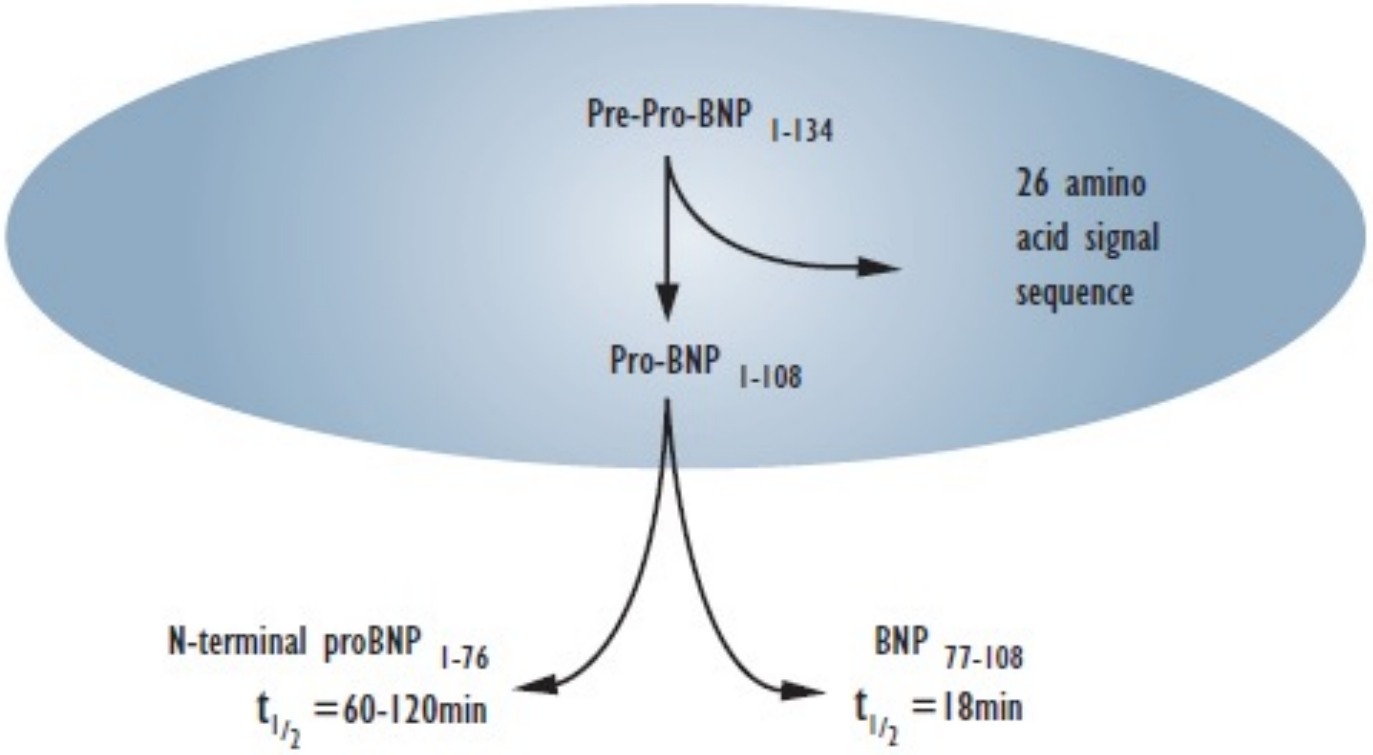
Cardiac Natriuretic Peptides

- What is BNP?
  - A 32 amino acid polypeptide
  - Belong to a class of structurally similar natriuretic peptides (classes A,B,C and D)
  - Secreted by cardiac myocytes (mainly left) in response to excessive distension of the Heart ventricles
  - Similar to ANP (Atrial Natriuretic Peptide) but has longer $t_{1/2}$ (~20mins, double that of ANP)
    Named after extracts found in Pig-brain
- What is NT-proBNP?
  - NT-proBNP is a biologically inactive 76 amino acid N-terminal fragment
  - Co-secreted with BNP
  - Even longer $t_{1/2}$ than BNP (~1-2hrs vs ~20mins)
- Biological effects of Cardiac Natriuretic peptides
  - Increase Natriuresis
  - Decrease peripheral vascular resistance
  - Overall reduce blood volume and therefore Cardiac Output

Synthesis in myocytes

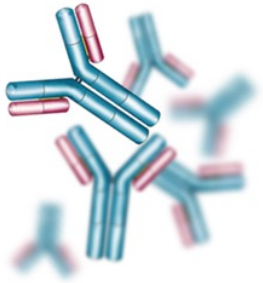
- Synthesis

Figure 1: Biology of NT-proBNP and BNP



Heart Failure Diagnostics

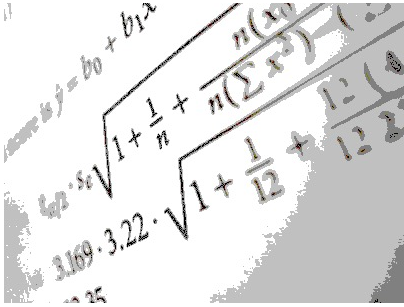
- BNP and NT-ProBNP
  - Assist in the diagnosis of Heart Failure (along with other tests and symptoms)
  - Can be used to 'grade' the Heart Failure based on concentrations found by assay
  - Useful in Prognosis
    - Poor prognosis typically consistent with higher blood concentrations
- When is the test ordered?
  - GP surgery or emergency setting I.e. Casualty/ER
- BNP/NTPro-BNP Assays
  - Require a fully automated immuno-assay methods
  - Immuno-assays are antibodies specific to different epitopes on the peptide chain
  - Selection of epitope design based on enzymatic cleavage considerations
  - BNP vs NTPro-BNP measurement have different advantages, I.e. due to $t_{1/2}$



Methods

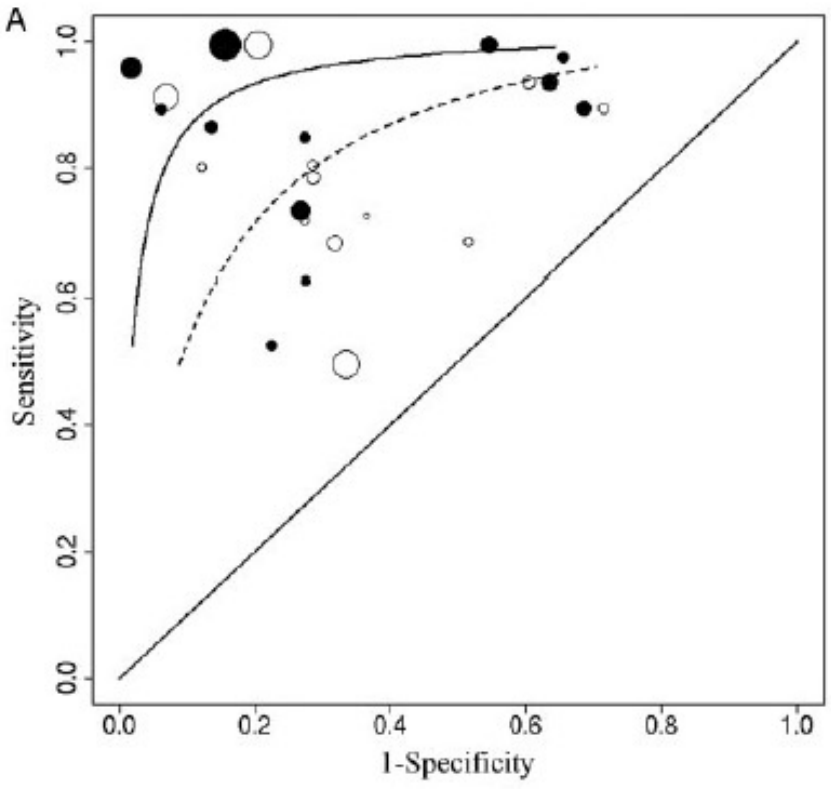
- Objective
  - *"To compare the diagnostic accuracy of brain natriuretic peptide (BNP) and the N-terminal part of BNP (NTPro-BNP) assays for the diagnosis of Heart Failure."*

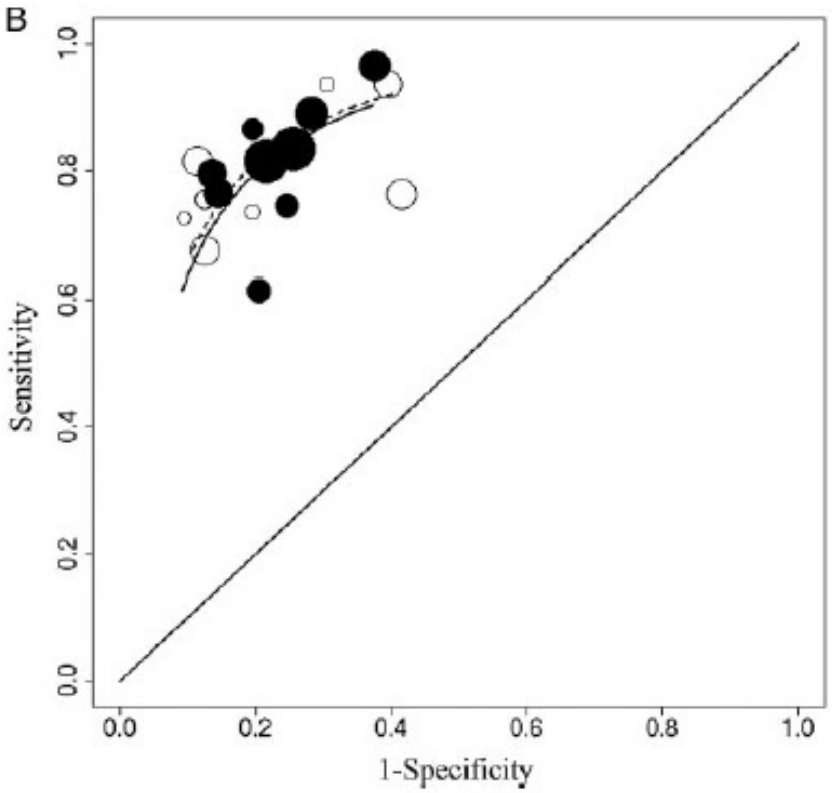
- Methods
  - A Meta-analysis by Clerico, Fontana, Zyew et al, published in Clinical Chemistry
  - Review contained only data generated by Parallel analaysis of Assays on same specimens
  - Used Area under the Curve (AUC), Diagnostic Odds Ratio, Reciever Operating Characteristic (ROC)
    - methods of deriving statistical conclusions from Gold standard and test under question in terms of specificity (true/false positives) and sensitivity.
  - %Specificity and % Sensitivity for each study in the analysis was converted to an overall score
    - This was performed for each study and categorised for Acute or Chronic HF
    - Conclusions for diagnostic accuracy drawn on group (Acute or Chronic) and marker (BNP vs NTPro-BNP)



Methods

- Moses type ROC curves (Sensitivity vs 1-Specificity)





Chronic HF

Acute HF

Solid lines/circles = NTPro-BNP
Dotted lines/circles = BNP

Results

- Statistical results
  - **(Table 1.0)** – A statistical comparison of diagnostic accuracy of markers BNP and NTPro-BNP in acute and chronic Heart Failure

Condition	Diagnostic Marker	
	BNP	NTPro-BNP
Acute HF	DOR Score = 16.46 95% CI (10.65-25.43)	DOR Score = 18.61 95% CI (10.65-25.43)
	Not significantly different	
Chronic HF	DOR Score = 8.44 95% CI (4.66-15.30)	DOR Score = 23.36 95% CI (9.38-58.19)
	Not significantly different	

Conclusions

- Statistical conclusions
  - ! There was some “dyshomogeneity” in the Chronic HF group results compared to Acute but this was not statistically significant – likely a result of greater homogeneity in acute Emergency setting
  - ✓ Both BNP and NT-ProBNP have a “high diagnostic accuracy”
  - ✓ Both are clinically relevant
  - ✓ Both are suitable for Acute and Chronic Heart failure diagnostics
- Theoretical conclusions
  - As BNP has shorter $t_{1/2}$ therefore in theory can reflect more recent ventricular status

References

- References used
  - 1. Comparison of the Diagnostic Accuracy of Brain Natriuretic Peptide (BNP) and the N-Terminal Part of the Propeptide of BNP Immunoassays in Chronic and Acute Heart Failure: A Systematic Review
  - 2. NT-pro-BNP – A New Test for Diagnosis, Prognosis and Management of Congestive Heart Failure
  - 3. Lab Tests Online
  - http://www.labtestsonline.org.uk/