# <sup>18</sup>F practical aspects

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## Outline

### Enriched water

### <sup>18</sup>F Fluoride and Fluorine work up

### Automation





### **Enriched** water

 $H_2^{18}O$  needed :  ${}^{18}O(p,n){}^{18}F$ 

Nuclear side reaction :  ${}^{16}O(p,\alpha){}^{13}N$ 

High enrichement, high <sup>18</sup>F yields

Expensive

### Recycling H<sub>2</sub><sup>18</sup>O via oxidation and distillation



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### **Enriched** water

Recycling possible :

KMnO<sub>4</sub> / NaOH for oxidising organic residues

Distillation

Nowadays not much done anymore : Lower prices and exchange with supplier



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# <sup>18</sup>F substitution reactions









## <sup>18</sup>F Work up

Extract <sup>18</sup>F from H<sub>2</sub><sup>18</sup>O Anion exchange : Biorad AG1-X8 in CO<sub>3</sub><sup>2-</sup> form More practical Seppak QMA or MN PS-HCO<sub>3</sub><sup>-</sup> Elute <sup>18</sup>F from ion exchange column with CO<sub>3</sub><sup>2-</sup> solution in water or mixture of CH<sub>3</sub>CN/water with PTC and K<sub>2</sub>CO<sub>3</sub>



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# <sup>18</sup>F Work up

No fluorination in presence of water

Azeotropic distillation with Acetonitril either under reduced pressure or normal pressure at 90-100 °C

"naked" fluoride impossible in organic solvent : Phase tranfer catalyst, PTC

Unreactive fluoride at glass surface



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### Philip





# Automation

Type of system

Reliability

Software

Flexibility

### Price





## Automation

3 principles :

Robot

Valves and vials

Kits





### Automation : Robot

Takes over manipulation inside hotcel

A few centers use these.

Advantage : flexibility and reliability

Disadvantage : costs and space

Use for routine and R&D



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Automation : Valves and vials Control the whole proces in one machine Uses valves, vials and tubing Advantage : complete system, relatively cheap Disadvantage : less flexible, less reliable More R&D character, 'home build' possible



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### Valves and vials

### First commercially available : Nuclear Interface













# Valves and vials



### bioscan





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# Valves and vials





### Raytest









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# Automation: Kit principle

Especially suited for production situation

One kit for one production

Advantages: No cleaning, dispose kit, reliable

Disadvantage: Not flexible



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# Automation Kit principle



### Coincidence GE Tracerlab MX



#### **Bioscan FDG**



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# **Automation Kit principle**

### **IBA Molecular**









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# Automation practical issues

Translation from hand synthesis to automated synthesis can be difficult

Cleaning is very important

Only selected valves and tubing work

Lot of tricks involved



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Automation considerations

Needed for protection

Only selected valves and tubing work

Software

GMP compliancy : in process control



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### **Purification tricks**

Fluoride binds strongly to Si and Al<sub>2</sub>O<sub>3</sub>

Apply Seppak cartridge : C18, Si or alumina

### HPLC





## **Purification tricks**





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### Purification tricks





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Purification tricks SPE formulation

Seppak C18, tC18, C8, tC8, C2 conditioned with sterile ethanol and water

Collect HPLC fraction in water at proper pH to trap Wash with sterile water Elute with sterile ethanol, sterile isotonic buffer

### Safe, no cross contamination, reliable, sterile



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