Effluents and Controls for FDG Production

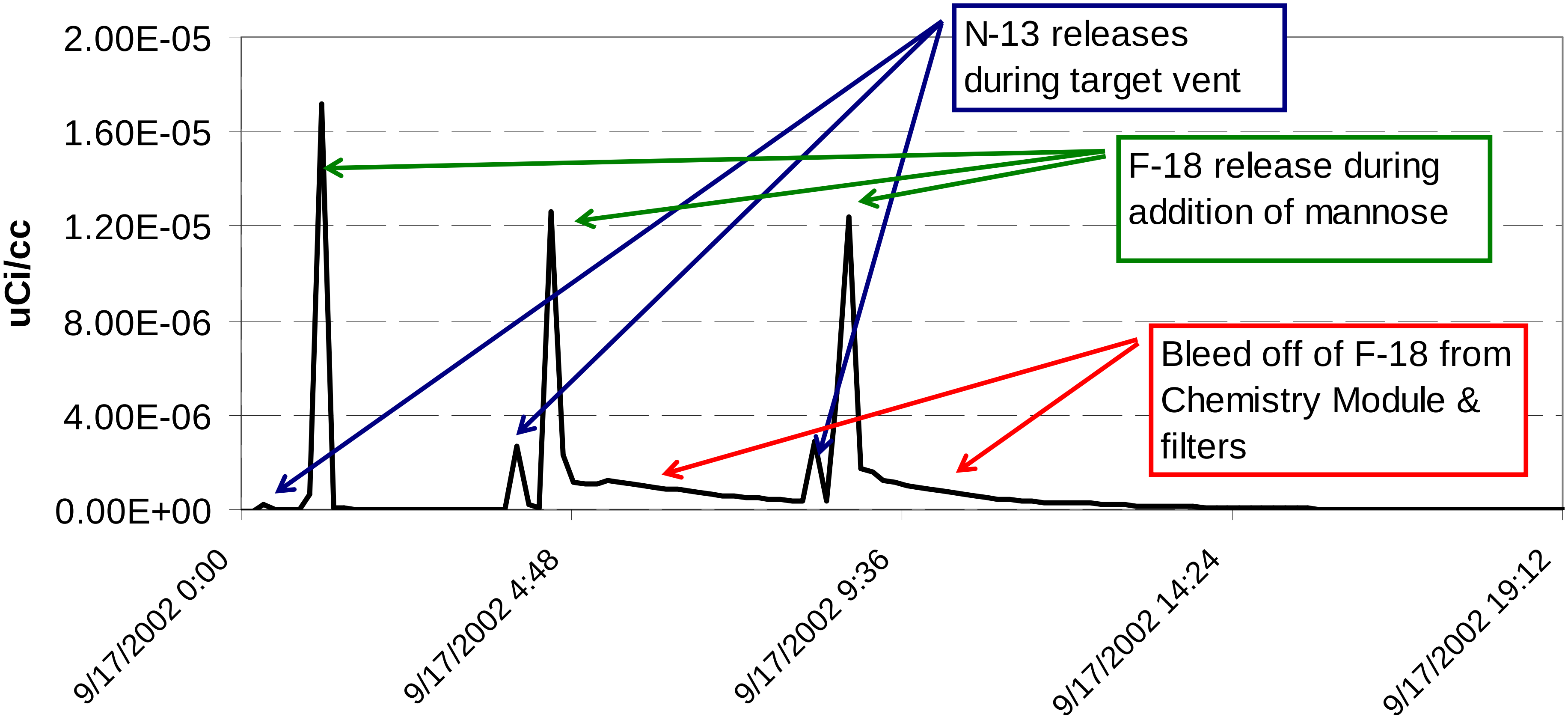
$[^{18}F]$[FDG] Production Effluent Composition

- Releases During Cyclotron Operation
  - Target Water between 80% and 96% ^{18}O
    - $^{18}O(p,n)^{18}F$
    - Remainder is ^{16}O
  - $^{16}O(p,alpha)^{13}N$
    - Chemical form – unknown but at least some fraction as N_2 gas – quantity very dependent on enrichment level
    - Released during venting of target prior to unload or in the event of target failure
  - Can be captured from target vent line

$[^{18}F]$[FDG] Production Effluent Composition

- Releases During Synthesis of FDG
  - Quantity depends on the efficiency of the chemistry and why the efficiency is less than normal
  - Chemical form
    - Hydrofluoric acid (HF)
    - Other fluorine compounds
  - Timing
    - Predominately occurs during addition of the mannose triflate to the dry fluoride ion

[^{18}F][FDG] Production Release Profile



N-13 releases during target vent

F-18 release during addition of mannose

Bleed off of F-18 from Chemistry Module & filters

Cyclotron Effluents

- Target or Line Failures
  - O-18 water targets
    - Much will get trapped in vacuum system but a sizeable quantity may go out the air exhaust
    - Very reactive and will plate-out along the duct
    - Gives a false release signal to stack monitor
  - Delivery or Load line failures
    - High levels of contamination in vicinity
    - Very reactive and will plate-out along the duct
    - Gives a false release signal to stack monitor

Controlling Effluents

- Filtration
  - Charcoal
    - Type
    - Quantity
  - HEPA
- Collection
  - Passive Collection (bags)
  - Active collection into compressed gas tanks

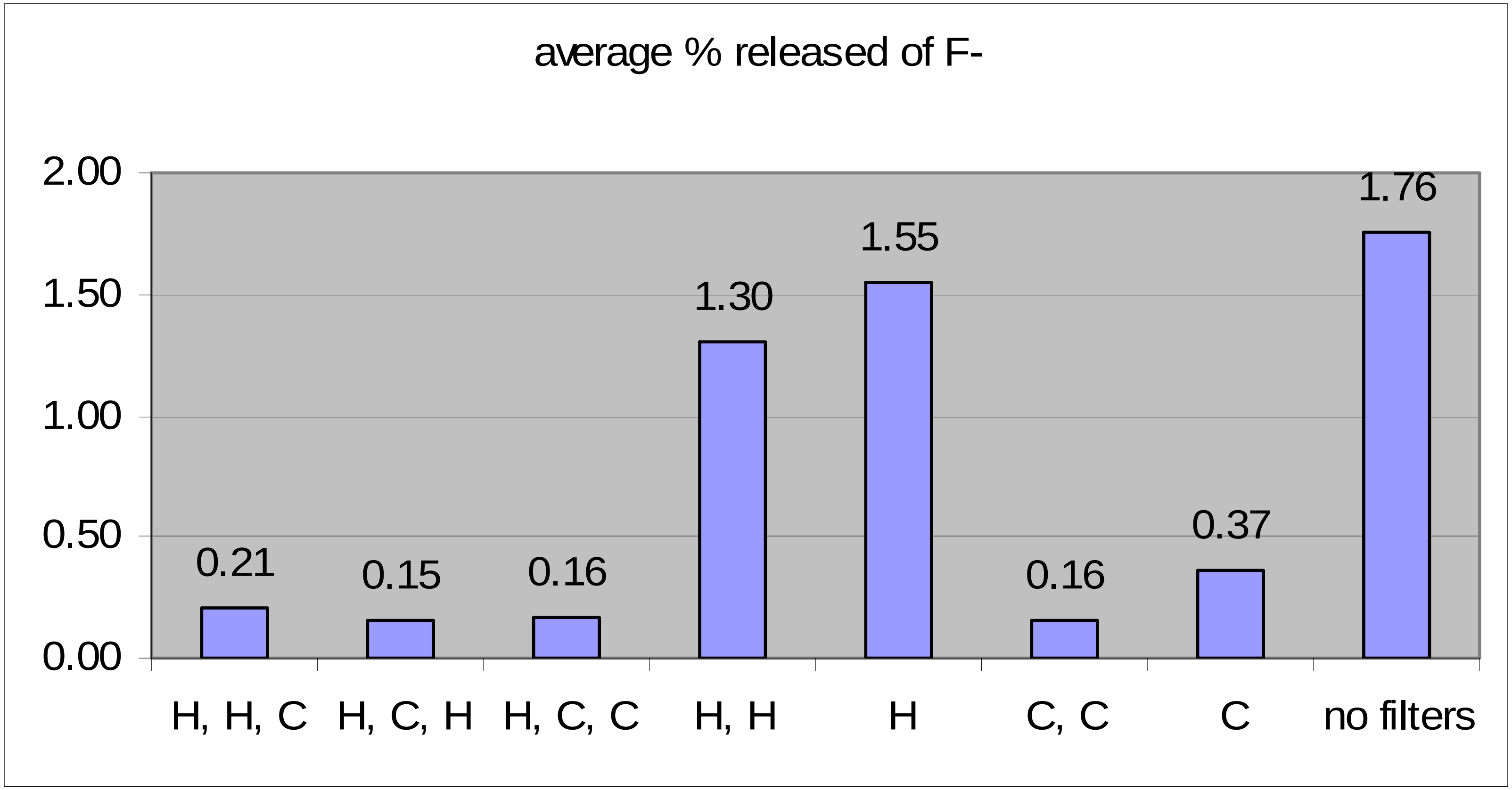
Design Phase

- Had to overcome mindset that releases weren't all that bad due to short half-life
- Some sites have nearby receptor points – increased public dose
- Some thought that a pound of carbon located on chemistry module was sufficient
- Necessary to ensure that new design was located so as to facilitate servicing by pharmacy personnel – not a very high priority previously
- Consideration of radiation fields from filter and impact on compliance with annual dose limits

Filtration Design Testing

- Original chemistry modules (open vessel) replaced by CI modules (closed vessel) and bagging begun
- Results muddied due to detector problems and change in chemistry modules
- Substantial reductions were achieved through combination of filtration and passive collection
- Next Step - Opted for a three cell housing design to evaluate combinations of HEPA and Carbon cells.
  - Testing with various filter types and numbers
  - Calculated collection efficiencies and unfiltered release fraction

Filter Test Results



Filter Shielding

- Measured 750 mR/h on contact with housing at carbon cell location during testing
- Shielded Enclosure (one inch lead) on four sides – enables placement essentially anywhere
- Should locate at floor level, and not on roofs or in ceilings, due to weight of carbon cell (~80 lbs) and shielding

New Filter Design Results

- Result from Site With New KEP3S Filter Installed
  - 93% drop in total activity released

	Before (Jan – Feb)		After (Mar – Jun)	
	Daily Ave (mCi)	Monthly Average (mCi)	Daily Ave (mCi)	Monthly Average (mCi)
Omaha	23	696	1.5	44.8

Additional Filter Design Criteria

- What requires filtration?
  - Chemistry modules
  - Hot cell
  - Cyclotron
- What does not require filtration?
  - QC process area

Additional Filter Design Criteria

- Cyclotron is a source of radioactive effluents that are partially amenable to filtration
  - Target Failure
    - ^{13}N as N_2 will not be filtered by HEPA or Carbon
    - ^{11}C as CO or CO_2 will not be filtered by HEPA or Carbon (some holdup of CO_2 on carbon has been seen)
    - Some ^{18}F will be mostly trapped in diffusion pumps or on inside of cyclotron – very reactive

Additional Filter Design Criteria

- Minimizing the total volume of air requiring filtration greatly reduces the size of the filters – but not possible if filtering cyclotron exhaust
- Residence time in the charcoal bed depends on air velocity and bed depth
- Larger carbon cells weigh upwards of 100 lbs each – increased risk of injury to personnel if not handled properly
    - Thought must be given to servicing
- Smaller overall dimensions aids in placement for pharmacies and reduces amount of shielding (and weight) required

Collecting Effluents (Passive)

- Closed vessel FDG chemistry modules lend themselves to passive collection of effluents via bags on exhaust port
  - Coincidence Technologies Module by GE
  - Explora Module by Siemens Molecular Imaging
  - Others?
- Modules use vacuum or pressure to move reagents and product from place to place

Collecting Effluents (Passive)

- Need chemically resistant materials (presence of HF acid)
- Currently using 10 liter Tedlar bags on CI modules
- Have also used Mylar balloons with good longevity – can be quite colorful!
- Collect exhaust from modules as well as delivery vial vent line (source of ^{13}N)
- Use two or more per module to allow for a full 10 half-life's of decay
- Need a shielded enclosure

Collecting Effluents (Passive)

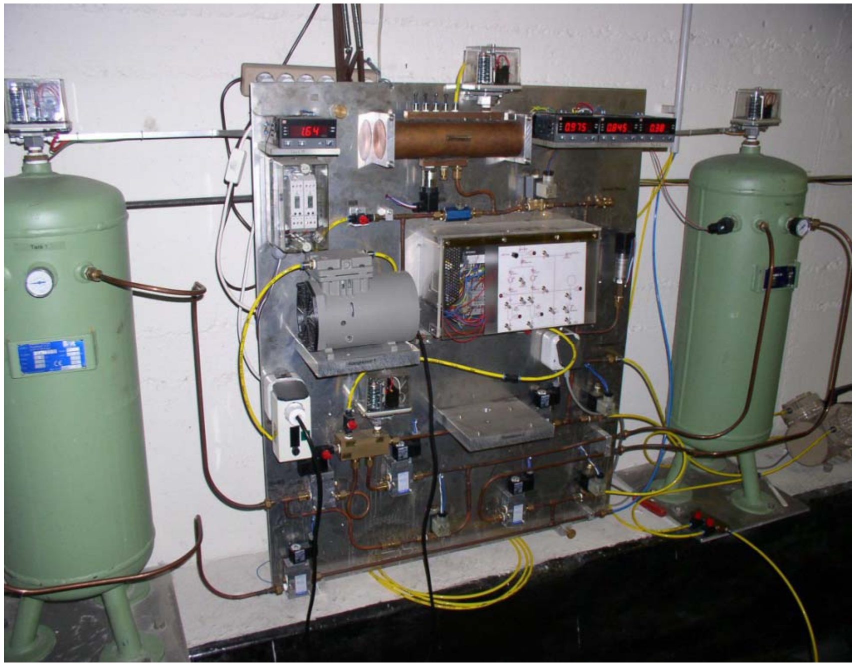
- Downside to passive collection systems
  - Bags eventually begin to leak
  - Realistically only small volumes collected
  - Require closed vessel chemistry modules
- Upside to passive collection systems
  - Low cost
  - Simple design

Collecting Effluents (Active)

- Use a system of pumps and collection tanks to pull and compress exhaust air.
- Control can be automated or manual
  - Use detector to sense presence of concentration above some threshold
  - Activate whenever module is on
  - Manual activation

Collecting Effluents (Active)

- Reviewed system at DESY PET in Hamburg, Germany that is based on detection of concentration > 0.5 MBq/m^3 (1.35*10^{-5} µCi/cc)
- Tank pressure ~ 100 psi max.



Collecting Effluents (Active)

- Use of detector based activation requires well shielded location to reach concentration threshold in duct
- Manual activation would need to be backed up by a visual or audible alarm
- Requires shielding
- Corrosion resistant container
- Careful design to eliminate chemistry problems caused by excessive backpressure or suction on exhaust port of module

Effluents and Controls for other PET Products

^{18}F Products other than FDG

- Ongoing work to study effluent release fractions for FLT, F-Dopa
- Currently a small fraction of production as compared to FDG
- Some products require use of F_2 gas target
  - Very reactive if ruptured
  - Use KEP3S filter system on cyclotron exhaust

^{11}C, ^{13}N, ^{15}O

- $^{11}CO_2$ easily trapped at point of collection using soda lime
- ^{11}CO, $^{13}NH_3$ & $^{15}O_2$ trapped using bags
- Delay lines can also be used

Effluent Monitoring

The Ideal PET Effluent Monitor

- Insensitive to “undesirable” radiation
- Easy to calibrate and verify operation
- Linear response
- Accurate
- Wide measurement range
- Stable under varying environmental conditions
- Simple display of results and an easy comparison to action levels for the end-user
- Compact
- Easy retrieval of stored data

Types of Detectors for In-Line Monitoring [^{18}F] [FDG] Effluents

- Flow-through Ion Chamber
  - Pros:
    - Somewhat insensitive to external radiation sources
  - Cons:
    - Difficult to calibrate in-situ
    - False readings due to loss of charge in the plates.
    - Disrupts airflow – this causes a flow rate dependent calibration factor
    - Operational experience very poor

Types of Detectors for In-Line Monitoring [^{18}F] [FDG] Effluents

- NaI(Tl) Scintillation Detectors
  - Pros:
    - Inexpensive
    - Commonly available
  - Cons:
    - Temperature dependence
    - Sensitive to nearby radiation sources
    - Higher background

Types of Detectors for In–Line Monitoring [^{18}F] [FDG] Effluents

- Plastic Scintillation Detectors
  - Pros:
    - Fairly inexpensive
    - Low temperature dependence
  - Cons:
    - Sensitive to nearby radiation sources
    - Higher background
    - Large size

Types of Detectors for In–Line Monitoring [^{18}F] [FDG] Effluents

- Combinations (GM + NaI, GM + Ion chamber)
  - Pros:
    - Covers a wider measurement range
  - Cons:
    - More expensive
    - Possibly sensitive to nearby radiation sources
    - Cross-over point

Types of Detectors for Off-Line Monitoring [^{18}F] [FDG] Effluents

- Potential for line losses due to the reactive nature of fluorine compounds.
    - Study being developed to quantify
- Short-half life would necessitate frequent sample collection media changes and counting or continuous counting.
- Some chemical forms can not be trapped on collection media.

Types of Detectors for Off–Line Monitoring [^{18}F] [FDG] Effluents

- Continuous monitoring works well using Laboratory Impex Systems
  - Pros:
    - Small size makes for easier installation in existing sites
    - Easy to shield if background issue
  - Con
    - Potential line losses – evaluating data recently received from LI

Thermo FHT 3511 Positron Stack Monitor

- Four plastic scintillation detectors operating in coincidence counting mode, energy windows & arranged on outside of duct.
- Standard PC running Windows® software for operation, display and data storage.
- Solid ^{68}Ge disk source for calibrations and operational verification.
- Data stored in an ACSII file

Thermo FHT 3511 Positron Stack Monitor

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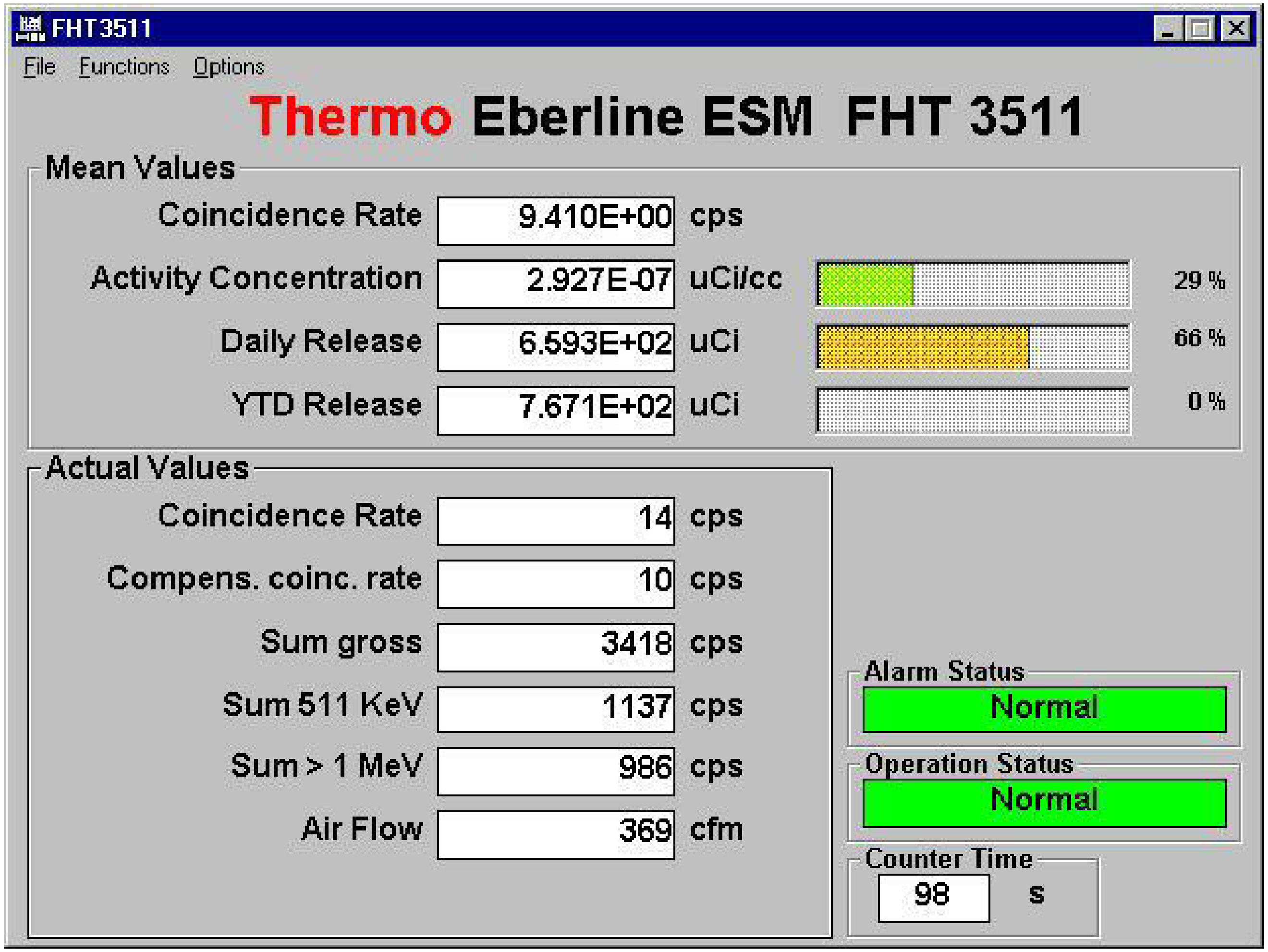


Thermo Eberline ESM FHT 3511

Mean Values

Coincidence Rate 9.410E+00 cps

Activity Concentration 2.927E-07 uCi/cc 29 %

Daily Release 6.593E+02 uCi 66 %

YTD Release 7.671E+02 uCi 0 %

Actual Values

Coincidence Rate 14 cps

Compens. coinc. rate 10 cps

Sum gross 3418 cps

Sum 511 KeV 1137 cps

Sum > 1 MeV 986 cps

Air Flow 369 cfm

Alarm Status: Normal

Operation Status: Normal

Counter Time: 98 s

FHT 3511 Type Calibration

- Released ^{18}F labeled fluoromethane into exhaust system for 3 to 5 minutes at a known rate.
- Fourteen releases ranging from $9.5*10^{-7}$ to $7.8*10^{-5}$ µCi/cc.
- Compared calculated concentration in duct to the displayed result.
- Factory Calibration factor was 2000 Bq/m^3/cps. Adjusted to 1430 Bq/m^3/cps.
- PETNET Calibration factor 740 Bq/m^3/cps based on F-18 releases

FHT 3511 Type Calibration

- Over-response at lower count-rates
- Possible Errors
  - Activity measurement
  - Release rate stability
  - Air flow measurement accuracy

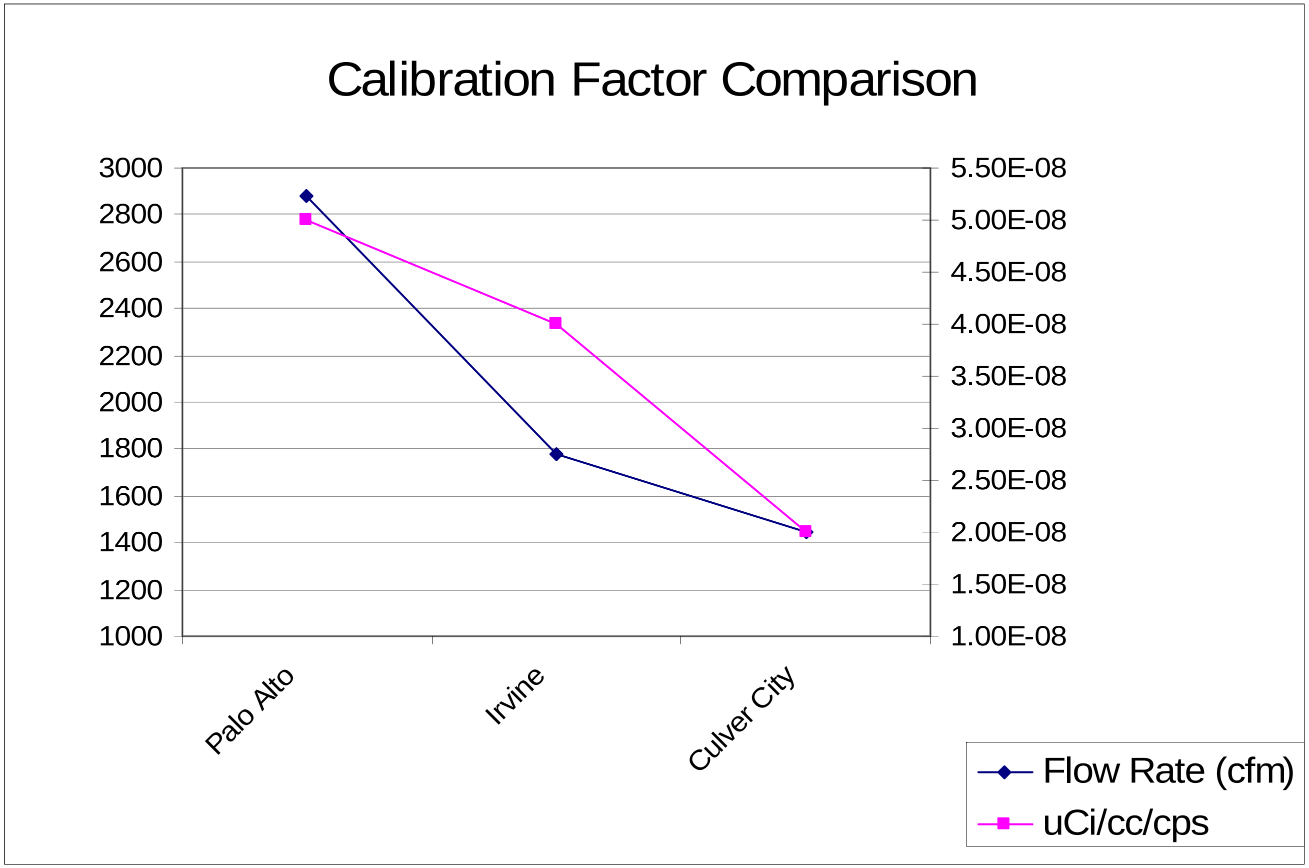
FHT 3511 Type Calibration

- Released $^{11}CO_2$ into exhaust system for 3 to 5 minutes at a known rate.
- Four releases ranging from 2.05×10^{-4} to 8.6×10^{-4} µCi/cc.
- Compared calculated concentration in duct to the cps.
- Calculated calibration factor 1480 Bq/m^3/cps (4.0×10^{-8} cps/µCi/cc)

Calibration of PET Effluent Monitors

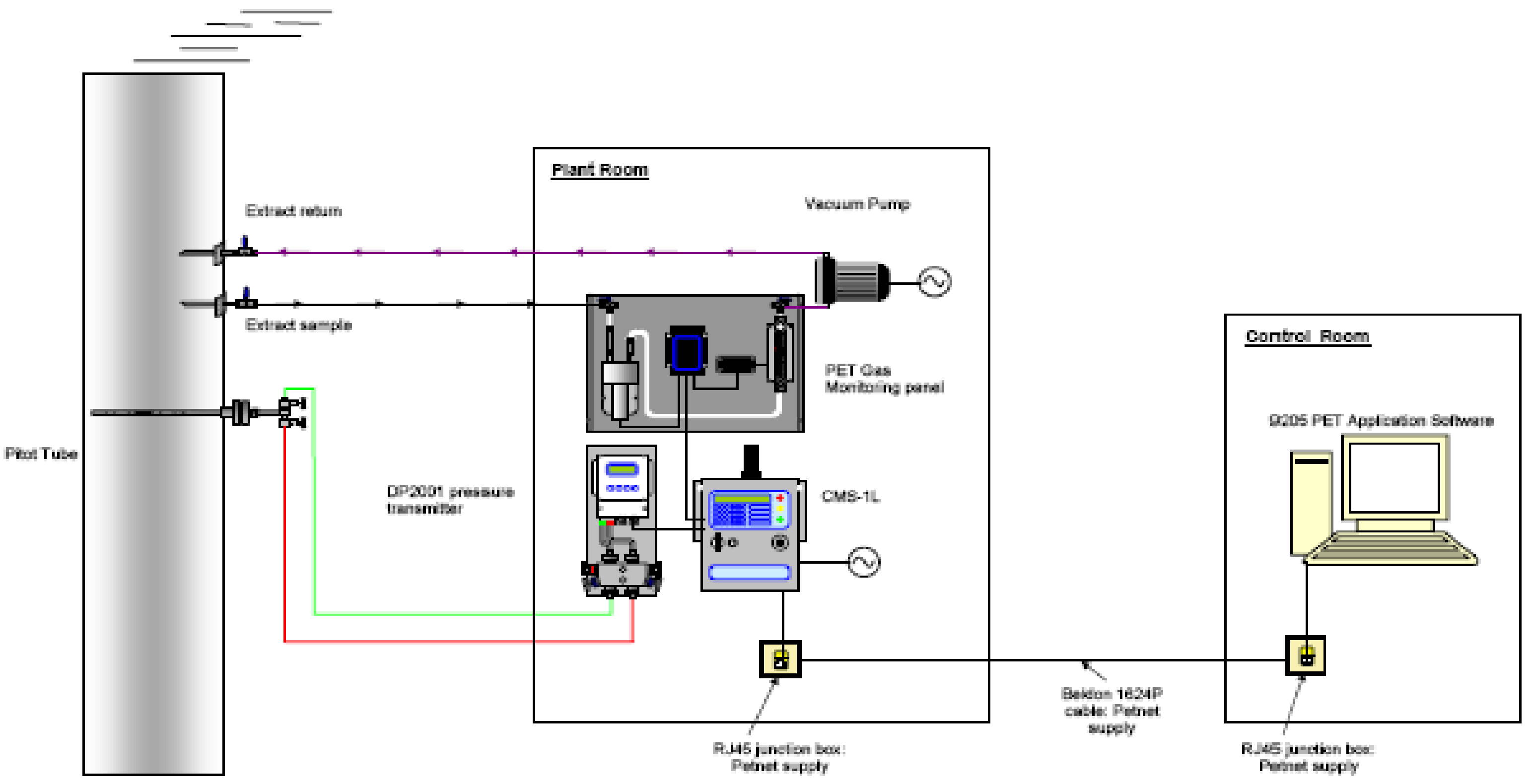
- Questions regarding flow rate dependence and applicability of solid source calibration for Thermo (Eberline) FHT3511 PET Effluent Monitor
- Repeated ^{18}F labeled fluoromethane releases at two other PETNET sites with differing flow rates
- Received formal calibration report from Thermo demonstrating validity of solid source for calibration purposes

Calibration of PET Effluent Monitors



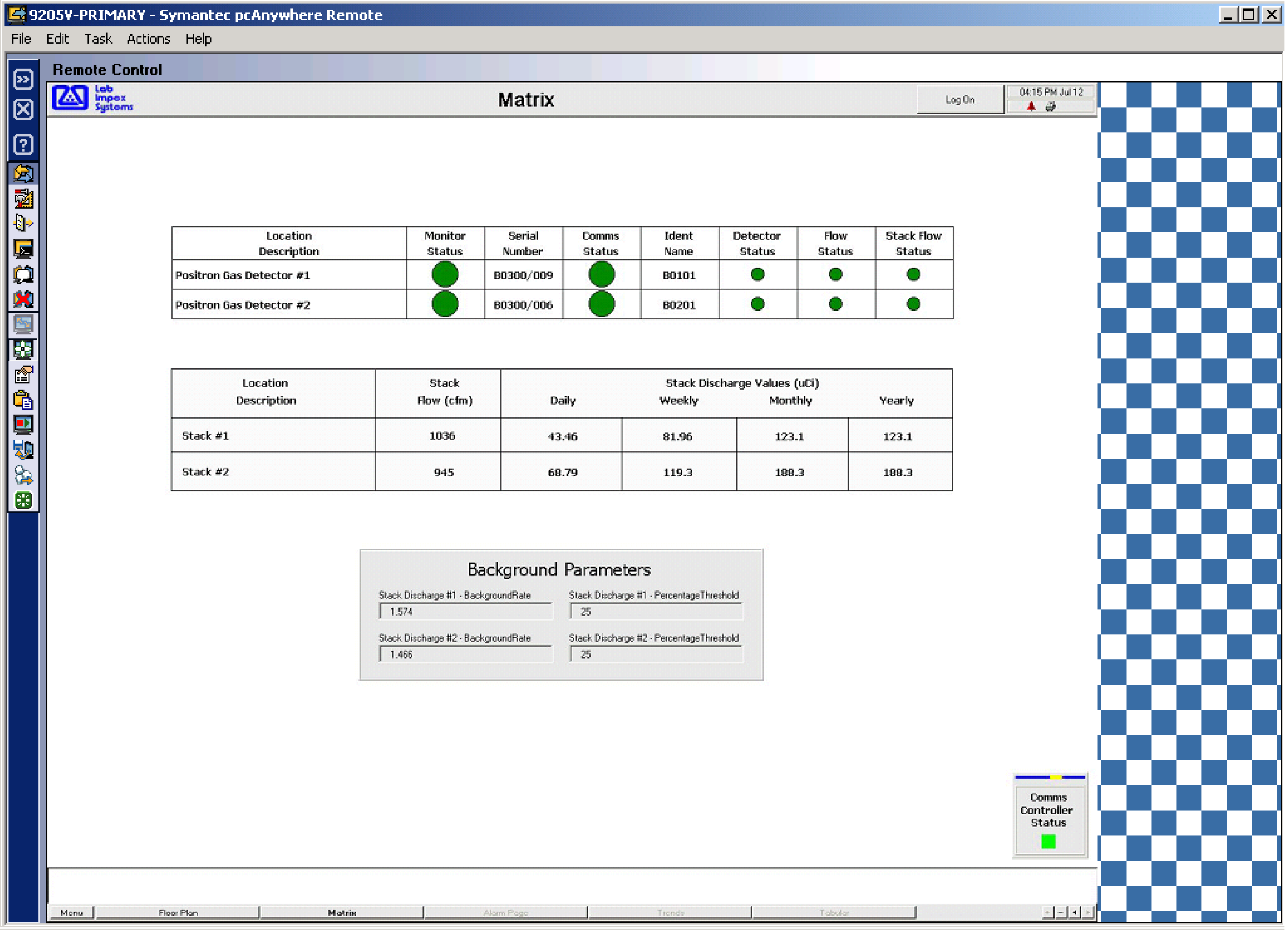
Lab Impex System Diagram

System Block Diagram of PET Monitoring System



REVISIONS	No.	Description	Checked	Approved	Date	Title	Drawn	Drawing Initially Created on
	1	Stack Monitoring System			02/20/04	PETNET Pharm. Stack Monitor	NC	02/20/04
						Drawing Number	Scale	Page 1 of 1
						NC/EXP/PETn/01	N.T.S.	

Lab Impex System Software



Matrix

Location Description	Monitor Status	Serial Number	Comms Status	Ident Name	Detector Status	Flow Status	Stack Flow Status
Positron Gas Detector #1	●	B0300/009	●	B0101	●	●	●
Positron Gas Detector #2	●	B0300/006	●	B0201	●	●	●

Location Description	Stack Flow (cfm)	Stack Discharge Values (uCi)			
		Daily	Weekly	Monthly	Yearly
Stack #1	1036	43.46	81.96	123.1	123.1
Stack #2	945	68.79	119.3	188.3	188.3

Background Parameters

Stack Discharge #1 - BackgroundRate: 1.574

Stack Discharge #1 - PercentageThreshold: 25

Stack Discharge #2 - BackgroundRate: 1.466

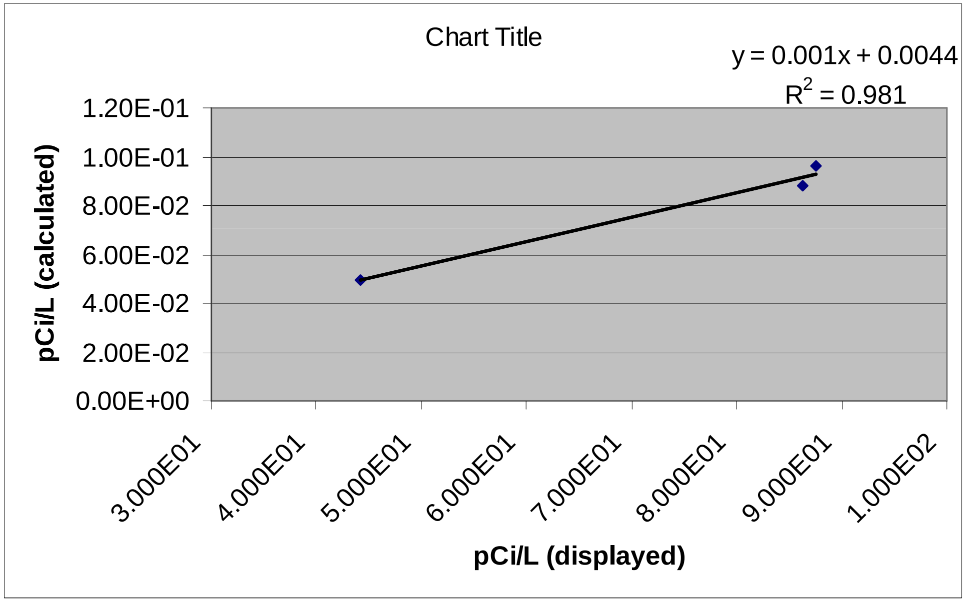
Stack Discharge #2 - PercentageThreshold: 25

Comms Controller Status ●

Lab Impex System

Laboratory Impex Calibration

- Used three releases of $^{11}CO_2$
- Compared calculated concentrations with displayed concentrations
- Looking to repeat over a broader range at another facility



PET References

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- Radionuclide and Radiation Protection Data Handbook 2002 (ICRU) – Radiation Protection Dosimetry Vol. 98 No 1, 2002

PET References

- Measurement and Control of the Air Contamination Generated in a Medical Cyclotron Facility for PET Radiopharmaceuticals – ORS May 2007
- Neutron Measurements in the vicinity of a Self-Shielded PET Cyclotron – Radiation Protection Dosimetry, Vol. 108, No. 3, pp. 255-261

PET References

- Shielding for a Cyclotron used for Medical Isotope Production in China - Radiation Protection Dosimetry, Vol. 115, No. 1-4, pp. 415-419
- Tantalum [^{18}O]Water Target for the Production of [^{18}F]Fluoride with High Reactivity…- Molecular Imaging and Biology, Vol. 4, No. 1, 65-70 2002

PET References

- Tritium in [^{18}O] Water containing [^{18}F]fluoride for [^{18}F]FDG Synthesis – Applied Radiation and Isotopes, 2004? (my file was a pre-publication copy)
- Decommissioning Procedures for an 11 MeV self-shielded Medical Cyclotron after 16 Years of Working Time – Health Physics, June 2006, Vol. 90, No. 6, pp. 588-596
- Various Carroll & Ramsey Associates Papers available on their website at http://www.carroll-ramsey.com/