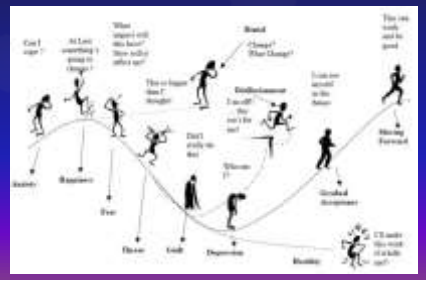
Implementation of MALDI-TOF in Clinical Microbiology

Michael Costello, Ph.D
Technical Director – Microbiology
ACL Laboratories
Mike.costello@advocatehealth.com

WSLH Teleconference
November 13, 2013

Matrix Assisted Laser Desorption Ionization – Time of Flight/Mass Spectrometry or MALDI-TOF/MS



Objectives

- A Microbiologist's view of MALDI-TOF/MS technology
  - Why are Laboratorians , Pharmacists, and Physicians so excited about this technology?
    - Faster, better, cheaper identifications of a wide range of microorganisms
- Thoughts on how this technology will change the practice of Clinical Microbiology
  - Benefits of decreased time to detection of pathogens
    - Directed patient care
    - Antibiotic stewardship
      - Right drug, right dose, for the right duration
  - Consistent and comparable results between Microbiology Labs and all shifts in the same lab
  - Fits well with automation – the next step
  - MALDI-TOF Vs. Molecular Testing
    - MALDI
      - Rapid, efficient identification from isolated colonies and liquids (MALDI-TOF/MS)
    - Molecular
      - Direct detection from patient specimens (Molecular)
      - Direct detection of resistance genes (MecA, VRE, CTX-M, KPC, NDM)

Objectives (Cont.)

- Summarize our experience with bioMérieux MS and Bruker MALDI-TOF/MS
  - Instruments comparable
    - Advantages will be in improved databases , data analysis, and middleware integration.
  - Expectations Vs. reality
    - Should be able to decrease the number of secondary identification systems required in Clinical Microbiology
    - Very good technology, but not perfect
    - Experienced technologists still needed
    - Better patient care through faster definitive results
    - Positive effect on workflow??

MALDI-TOF MS: History

- Developed in 1980s by Karas and Hillenkamp
- Detection of large molecules using TOF by Tanaka and Yoshida
- Introduction of matrix compounds to analyze large molecules

- First commercial instrument developed by Shimadzu
- First commercial database developed by Anagnostec (1998)
- Shimadzu scientist receives Nobel Prize in Chemistry
  - Kiochi Tanaka (2002)
- Technology in use in Europe for >10 years.

MALDI-TOF/MS – WHY CHANGE?

Factor	Traditional ID	MALDI ID
Decreased time to ID, should translate into better, more cost effective care. •Faster ID should limit nosocomial infections. •Better use of isolation beds. •Address pressure to reduce TAT	++(rapid methods faster)	++++ (Definitive ID)
Training required - Different/additional skill set required. (Pipetting 1 µL, computer skills)	++++ (more)	++ (Less, different skill set)
LEAN (anaerobes, blood cultures, Mycology, Mycobacteriology, routine)	++ (less LEAN) Results need to make sense	+++ (more LEAN) Results need to make sense!
Different technology, different IDs [Anaerobic GPC (*Finegoldia magna, Peptococcus acidfactica*), coagulase negative Staph, anaerobes, nonfermentors, others (*Lysinibacillus* Sp.)]	++ (mature technology, changes linear)	New technology (Proteomics) IDs are database dependent
Equalizer of expertise between shifts and Labs. All give comparable results. ID is database driven.	++	++++

FASTER, BETTER, CHEAPER!

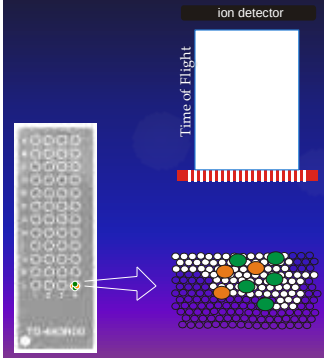
MALDI – TOF/MS EVALUATION STUDIES

Factor Driving Switch from Biochemical to MALDI-TOF Bacterial Identification

- **Most significant advance in Clinical Microbiology in 25 years!**
  - **Rapid and cost effective identification of bacteria directly from isolated colonies and positive culture bottles based on protein biomarkers**
    - Protein biomarkers measured are highly expressed proteins responsible for housekeeping functions, such as ribosomal (16S) and transcription/translation factor proteins

FASTER, BETTER, CHEAPER, BUT NOT PERFECT!

MALDI-TOF MS: Basic Principles

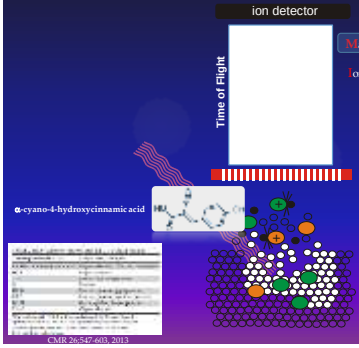


in vacuum
$< 10^{-7}$ Torr

α-cyano-4-hydroxycinnamic acid

analyte molecules incorporated in matrix crystals
- matrix adsorbs UV light

MALDI-TOF MS: Basic Principles



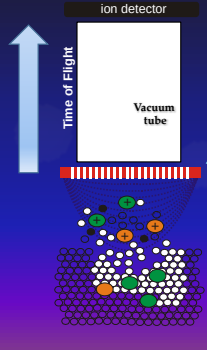
Matrix Assisted Laser Desorption
Ionization–Time of Flight/Mass Spectrometry

laser pulse:
- desorption of matrix and bacterial proteins
- ionization by charge/energy transfer

CMR 26:547-603, 2013

Courtesy of bioMérieux

MALDI-TOF MS: Basic Principles



Matrix Assisted Laser Desorption
Ionization–Time of Flight/Mass Spectrometry

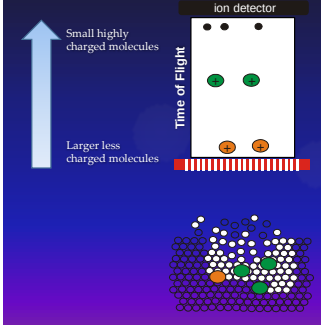
Ring electrode

build-up of an electromagnetic field

acceleration of ions

Courtesy of bioMérieux

MALDI-TOF MS: Basic Principles

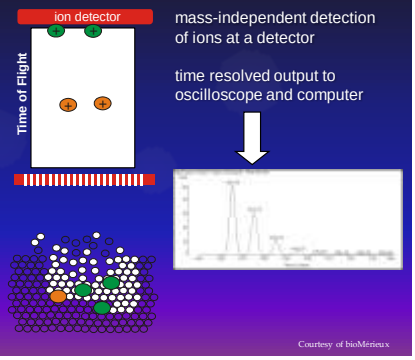


separation of ions in a field free drift range of a fixed length by velocity (**T**ime **O**f **F**light)
L ≈ 1 m

Matrix Assisted Laser Desorption
Ionization–Time of Flight/Mass Spectrometry

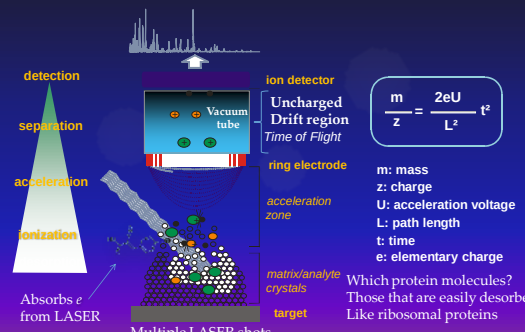
Courtesy of bioMérieux

MALDI-TOF MS: Basic Principles



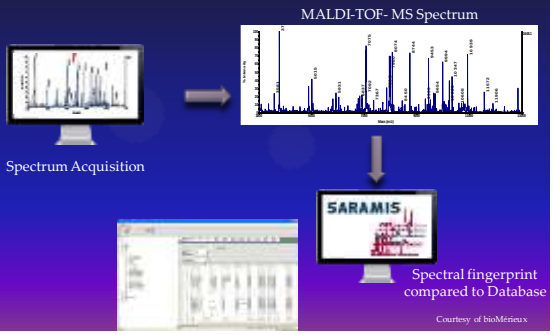
Courtesy of bioMérieux

MALDI-TOF MS Overview



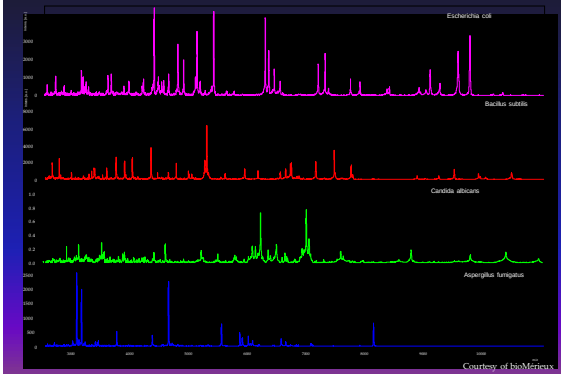
Courtesy of bioMérieux

Data Interpretation



Courtesy of bioMérieux

MALDI-TOF SPECTRA



Courtesy of bioMérieux

Candida dattila

Lysinibacillus fusiformis

Candida utilis

Corynebacterium aurimucosum

Preparation for MALDI-TOF

MALDI-TOF Issues

Trichosporon inkin

New Technology – New Names, Few CLSI Breakpoints

Pediococcus parvulus

Finegoldia magna

Propionibacterium propionicum

Eggerthella lenta

PATIENT HISTORY

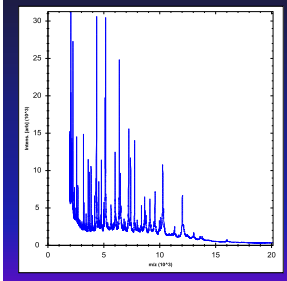
83 year old "questionably competent" man, living by himself in a rural area near Burlington, WI. was brought in by Social Services for evaluation of cellulitis in right leg.

- Physical exam – Ulcerations and maggot infected wounds on his right leg and groin area. Wounds cleaned and patient placed on Zosyn
  - Mild erythema and shallow ulcerations consistent with venous disease
  - No history of fever, chills. etc., but patient was not a reliable historian
- Labs
  - WBC count 8500 mm^3 (85% PMNs)
  - Hgb/Hct 9.0/28.5
  - Glucose 255 mg/dL
- Discharge
  - Wounds clean and granulating (healing)
  - Patient referred to Social Services due to inability to take care of himself

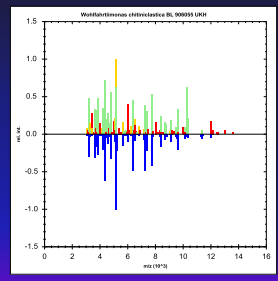
MICROBIOLOGY WORKUP

- Wound and blood cultures taken
  - Blood cultures were negative
  - Wound cultures yields a Gram negative rod at 24 hours
    - BAP colonies were gray-white, convex, smooth, with minimal spreading at 24 hrs. No growth on MAC at 24 hrs., pinpoint growth at 48 hrs.
    - Vitek 2 – No ID
    - Microscan – *Oligella* Spp., with low accuracy
    - API 20 NE
      - *Brevundimonas diminuta* or *Oligella* Spp. (~70% accuracy)
    - GNR susceptibility set up
    - Bruker MALD-TOF - *Wohlfahrtiimonas chitinclastica* (2.43)
  - Sent to ARUP for sequencing (16S rDNA) and 10 days later
    - *Wohlfahrtiimonas chitinclastica*

Wool farti – What!??



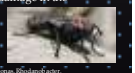
Spectra



Spectra comparison

Wohlfahrtiimonas chitinclastica

- Gram-negative, regular, non-motile rods. Strictly aerobic. Catalase and oxidase reactions are positive. Strong chitinase activity
- Type strain, isolated from 3rd stage larvae of Wohlfahrtia magnifica
  - ***Wohlfahrtia magnifica*** (spotted flesh fly) occurs in the Mediterranean basin, Near East, and Central and Eastern Europe. Not reported in U.S.
    - most important myiasis-producing fly affecting camels
    - Cause of myiasis in other mammals, mainly in sheep, but also in cattle, goat, horses and rarely in human
  - In *Cochliomyia* and *Wohlfahrtia* infestations, larvae feed in the host for about a week, and may migrate from the subdermis to other tissues in the body, often causing extreme damage in the process.
- Class: Gammaproteobacteria
  - Order: Xanthomonadales
    - Family: Xanthomonadaceae
      - (Asprosonas, Luteibacter, Silanimonas, unclassified_Xanthomonadales, Aquimonas, Dokdonella, Thermomonas, Arenimonas, Rhodanobacter, Lysobacter, Pseudoxanthomonas, Ultramonas, Dyella, Pseudoxanthomonas, Frateuria, Fulvimonas, Ignavibacteria, Xanthomonas, Xylella)
      - Genus: Wohlfahrtiimonas
  - Habitat
    - Fly larvae
  - Disease association
    - Low pathogenicity, most commonly seen in debilitated or homeless individuals
      - 60 year old homeless person with open sores. Marseille, France (EID 2009: 15;985)
      - 70 year old homeless male with open sores. Buenos Aries, Argentina (JCM 49; 2011:2333-2335)
      - 83 year old male "questionably competent" with open sores. – Burlington, WI



Summary - *Wohlfahrtiimonas chitinclastica*

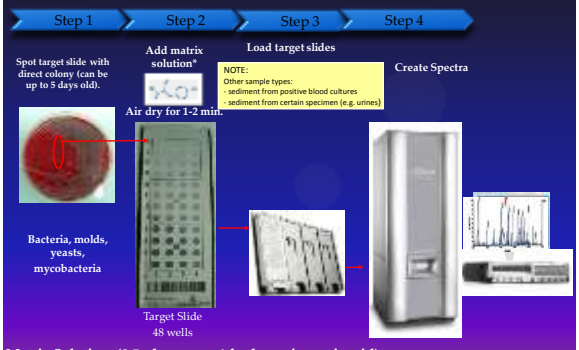
- MALDI-TOF gave correct ID within 30 hours of culture collection
  - ID not reliable using conventional methods
  - Sent to referral lab for Sequencing - took 10 days
- Literature review
  - Associated with open sores in debilitated or homeless individuals
    - Limited pathogenicity
    - ***Wohlfahrtia magnifica*** not reporting in U.S.
      - Another vector?
  - Very sensitive to β-lactams, aminoglycosides, flouroquinolones.

Additional Microorganisms Identified By MALDI-TOF – Partial List

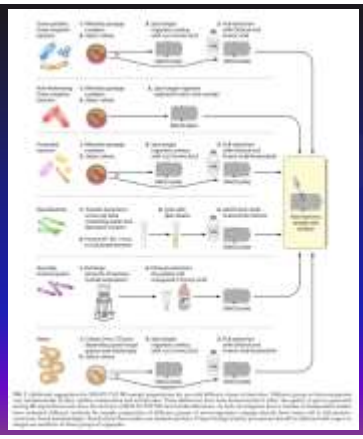
- **Nonfermenters**
  - *Achromobacter denitrificans, Actinomyces europaeus,*
- **Diptheroids**
  - *Arthrobacter cumminsii, Propionibacterium propion*icum
- **Anaerobic Gram positive Cocci**
  - *Finegoldia magna, Globicatella sanguinis, Parvimonas micra, Peptoniphilus indolicus, Pediococcus parvulus*
- **Gram positive bacilli**
  - *Aneurinbacillus aneurinilyticus, bacillus atrophaeus, Bacillus badius, Bacillus simplex, Bacillus sporothermodurans, Carnobacterium divergens, Carnobacterium maltaromaticum, Clostridium fallax, Clostridium tyrobutyricum, Collinsella aerofaciens, Corynebacterium aurimucosum, Corynebacterium auris, corynebacterium bovis, Eggerthella lenta, Geobacillus thermodenitrificans, Lysinibacillus fusiformis, Lysinibacillus sphaericus, Weissella confusa, Virgibacillus pantothenticus,*
- **Gram negative bacilli**
  - *Arcobacter cryaerophilus, Campylobacter sputorum spp., Capnocytophaga ochracea, Capnocytophaga sputigena, Delftia acidovorans, Raoultella terrigena, Proteus hauseri*
- **Yeast**
  - *Candida dattila, Candida hellenica, Candida melibiosica, Candida norvegica, Candida silvicola, Candida valida, Cryptococcus humicola, Crypotcoccus curvatus,* ***Cryptococcus gattii****, Debaryomyces carsonii, Saccharomyces kluyveri*

MALDI-TOF Workflow Overview

MALDI TOF Sample Preparation



Matrix Solution: (0.5 µl α-cyano-4-hydroxycinnamic acid)



CMR 26:547-603, 2013

MALDI-TOF MS Time Studies

Workflow step	Time (min)		
	n = 5 isolates	n = 24 isolates	n = 96 isolates
Application on plate	1	5	16
Application Matrix	1	3	10
Drying	2	2	7
Read in system	5	12	43
Time to result			
Total	9	22	76

*bioMérieux testing done in association with Limbach Labs, Germany

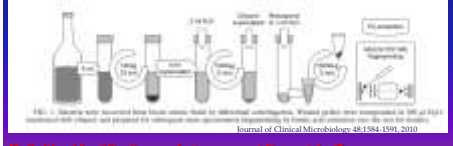
Benefits of Rapid Positive Blood Culture Identifications

Direct Detection for Positive Blood Culture Bottles By MALDI

Purpose: Separate human and bacterial/yeast ribosomal proteins
Methods: Lysis/centrifugation or membrane filtration

Journal of Clinical Microbiology 51:805-809, 2013

Issues:
- Removal of human proteins
  - Extraction protocol required
- Bacterial concentration
  - need~10^5/mL
- Polymicrobial specimens
  - Seen on Gram stain?
- Charcoal
- Antibiotic resistance genes
- Yeasts?
- Unique database, different cutoffs?



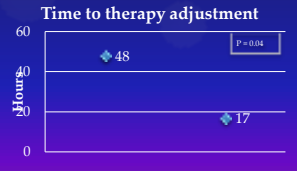
Journal of Clinical Microbiology 48:1584-1591, 2010

Bruker Sepsityper Kit

Definitive identifications as fast as current Gram stains?

Impact of MALDI-TOF MS Study from Methodist Hospital, Huston TX

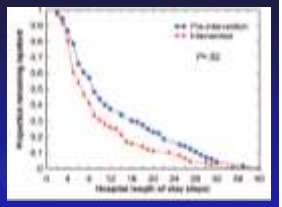
- Intervention arm (Gram Negative Bacilli):
  - Integrated rapid ID with active antimicrobial stewardship
  - **Results called to infectious diseases pharmacist 24/7**
  - Pharmacist recommends de-escalation or adjustment of therapy based on the rapid ID
  - Time to adjusted therapy was significantly reduced by 31 hrs.



Perez KK, et al. Arch Pathol Lab Med. 2012

EFFECTS ON HEALTH CARE COST

- Hospitalization cost reduction of $19,547/patient
- Estimated cost savings of ~ $18 million annually



Perez KK, et al. Arch Pathol Lab Med. 2012

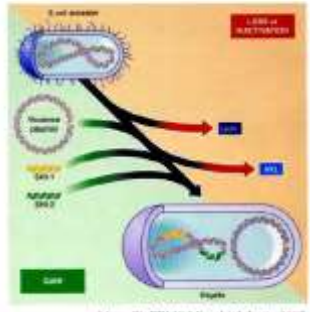
MALDI-TOF Issues

No Test Is Perfect

- ***E. coli* Vs. *Shigella***
  - Very closely related and cannot be differentiated
  - Molecular methods
- ***Streptococcus pneumoniae* Vs. *Streptococcus mitis* group**
  - Very closely related, new databases can give a definitive ID
  - Differentiate by Bile solubility or optichin disk
- ***Bordetella pertussis* Vs. *Bordetella bronchioseptica***
  - Very closely related and cannot be differentiated
  - Rarely cultured

Escherichia coli vs *Shigella*

- ***Shigella* spp. and *E. coli* K12 have 93% of genes in common.**
- **Differences:**
  1. Acquisition of virulence plasmid.
  2. Acquisition of two chromosomal pathogenicity islands.
  3. Alteration of genes that hinder infection.



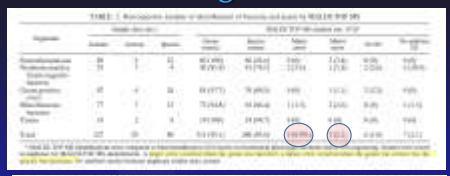
Marcelli, FEMS Microbiol. Lett., 2007

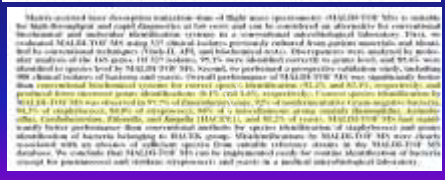
No Test Is Perfect

- ***Stenotrophomonas maltophilia* Vs. *Pseudomonas hibiscola, Ps. gentculata, Ps. betelli***
  - Very closely related and cannot be differentiated
  - Biochemical ID required
- The ***Acinetobacter baumanii-calcoaceticus complex*** (*A. baumanii, A. calcoaceticus, A. genospecies 3, A. genospecies 13*):
  - Species differentiation can be difficult.
    - ***A. baumanii* and *A. calcoaceticus* can be differentiated**, there are several members of the "Genospecies 3" clustering with *A. baumanii* or *A. calcoacteticus*, this can lead to "A. genospecies 3" ID result where biochemistry will identify *A. baumanii* or *A. calcoaceticus*

Vitek MALDI-TOF/MS Evaluation

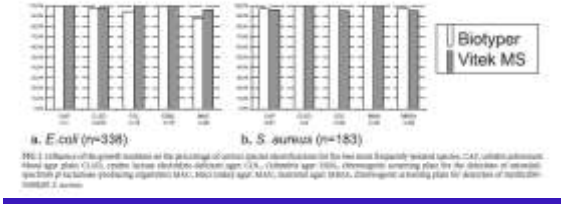
Setting Goals





Goals: <2% Major errors and <5% Minor errors – Better than Vitek2 or Microscan

Influence of Growth Media



JCM 2012; 50;1313.

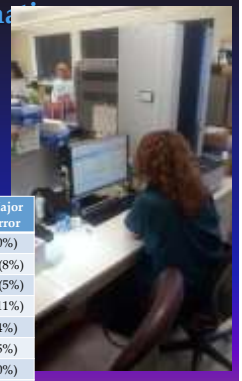
Evaluation Summary – Vitek MS

Bacteria	#	No ID	Minor Error	Major Error
Streptococcus	160	5 (3.1%)	5 (3.1%)	2 (1.3%)
Staphylococcus	171	2(1.2%)	0 (0%)	1 (0.6%)
Enterobacteriaceae	392	43 (10.9%) 10 (2.6%)	40 (10.2%)	4 (1.0%) 2 (0.5%)*
Fastidious GNR	27	4 (14.8%) 2 (7.4%)	2 (7.4%)	0 (0%)
Anaerobes	109	11 (10.1%) 6 (5.5%)	4 (3.7%)	4 (3.7%)
Nonfermenters	130	10 (7.7%) 6 (4.6%)	13 (10.0%)	3 (2.3%)
Corynebacterium	23	3 (12%) 1 (4.3%)	0 (0%)	1 (4.3%)
Yeast	64	3 (4.7%)	1 (1.6%)	0 (0%)
Totals	1076	76 (7.4%) 35 (3.3%)	56 (5.4%)	13 (1.3%)

* Not including *Shigella flexeri* and *Shigella sonnei*

Microbiology Lab Automation – Bruker MALDI-TOF

- Evaluation in progress at WAMH
- Selection of automation dependent on MALDI-TOF selection
- Burker integrates best with BD or Siemens
- bioMérieux MALDI-TOF integrates best with bioMérieux products



Bacteria	#	No ID	Minor Error	Major Error
Streptococcus	130	15 (11%)	26 (20%)	0 (0%)
Staphylococcus	147	3 (2%)	9 (5%)	12 (8%)
Enterobacteriaceae	435	12 (3%)	37 (8.5%)	20 (5%)
Fastidious GNR	18	1 (5%)	1 (5%)	2 (11%)
Anaerobes	52	3 (6%)	7 (22%)	2 (4%)
Nonfermenters	116	4 (3%)	18 (15%)	6 (5%)
Yeast	22	0 (0%)	0 (0%)	0 (0%)
Totals	898	38 (4%)	98(11%)	42 (5%)

Evaluation Results

- MALDI-TOFs are comparable
- Selection should depend on your laboratories requirements.
  - Current equipment
  - Middle ware
  - Volumes – Identifications/hour

Growth Requirements for MALDI Identification

The perfect MALDI Media:
- Support growth of all pathogens
  - Gram positive, Gram negative, aerobes, anaerobes
- Small, well separated colonies
- No "swarmers" allowed

Pre MALDI - Good Clinical Microbiology Begins With Good specimens – Garbage In = Garbage Out

- **Control of sample acceptability**
  - Verification that appropriate sample(s) collected
  - Correct volume submitted
  - Sample placed promptly in correct transport media
  - Optimal and timely transport conditions
  - Sample handled properly in laboratory
    - Shared samples
    - Reflexed samples

MALDI-TOF Vs. Current Identification Methods

	Tube Biochemicals	API	Rapid ID Methods	Automated Identification	Real-Time PCR	Mass Spectrometry
Sensitive and Specific	✓	✓✓	✓✓	✓✓	✓✓	✓✓✓✓
Rapid			✓✓✓	✓	✓✓	✓✓✓✓
Easy to perform	✓✓	✓✓	✓✓✓	✓✓✓	✓✓	✓✓✓
Easy to interpret		✓	✓✓	✓✓	✓	✓✓✓✓
Cost Effective	✓✓✓	✓✓	✓✓✓	✓✓	✓	✓✓✓✓
High Through-Put			✓✓	✓✓✓	✓✓	✓✓✓
Use with multiple organism types			✓	✓✓	✓	✓✓✓
Able to interface to LIS				✓✓	✓	✓✓
Can be automated				✓✓		✓✓✓✓

MALDI-TOF/MS – WHY CHANGE?

Factor	Traditional ID	MALDI ID
Antibiotic Stewardship (right antibiotic and the right time)	++	+++? Will rapid IDs change Rx? E. Coli Vs. P. aeruginosa
Reduce need for repeat IDs on different systems. Reduce secondary ID systems	More	Less (?)
Bioterrorism Select Agent Identification	+ (rule out)	+++ (rule in?)
Automation. (Specimen prep. Total automation)	++	++++
Lessen potential for contamination	++	+++ (less manipulation)
Medical Waste	+++	+
Cost – To Microbiology (Equipment, reagent, and personnel costs)	More (ROI 2-5 years)	Less
Cost – To Health Care System - Use of beds, cost of inappropriate testing, nosocomial infections	More	Less
FDA approval	Yes	In progress

CAP Requirements
CAP Microbiology Checklist – 7/29/13

MATRIX-ASSISTED LASER DESORPTION IONIZATION TIME-OF-FLIGHT (MALDI-TOF) MASS SPECTROMETRY

This section applies to laboratories using MALDI-TOF systems to perform organism identification. Refer to the Test Method Validation section in the All Common Checklist for validation requirements pertinent to laboratory-developed tests.

"NEW" 07/29/2013
MIC.16575 Instrument Operation Phase II

Procedures are documented for operation, calibration and maintenance of the mass spectrometer.

"NEW" 07/29/2013
MIC.16585 Instrument Maintenance Phase II

The documented procedure requires that the mass spectrometer be maintained at regular intervals as suggested by the manufacturer, or if different criteria or procedures from the manufacturer are used, these procedures have been validated and the records maintained on file.

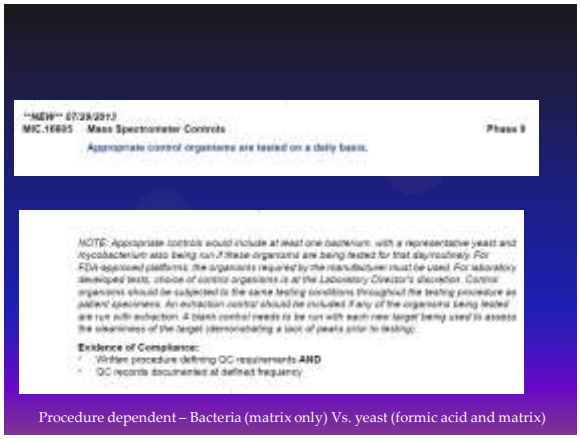
Evidence of Compliance:
- Records of instrument maintenance

"NEW" 07/29/2013
MIC.16595 Mass Spectrometer Calibration Phase II

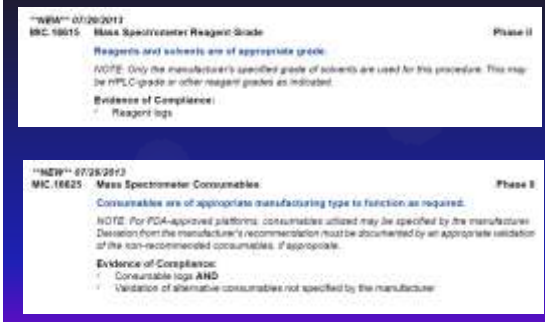
A calibration control is run each day of patient/client testing, with each change in target plate, or according to manufacturer's recommendations and these records are maintained.

NOTE: Acceptable tolerance limits for calibration parameters must be defined, and records maintained.

Evidence of Compliance:
- Records of calibration



Procedure dependent – Bacteria (matrix only) Vs. yeast (formic acid and matrix)



Tooth picks Vs. Culture Loops

MALDI Phase In Approach
Current Uses of MALDI-TOF at ACL

- Blood cultures
  - Not yet identifying blood culture pathogens directly form bottle. Still plating positive blood cultures.
    - MALDI ID done from isolated colonies
      - Time to ID decreased by 16-24 hrs.
- Anaerobic cultures
  - Anaerobes are now go for 72 hours before evaluation of plates.
    - Colonies are identified by MALDI
      - No aerotolerence testing
      - Aerobic and anaerobic cultures used to be read together, but not required with MALDI.

- Until specific CPT codes come out for the MALDI, use the following (same as current)
- Anaerobe ID 87076
- Aerobe ID 87077
- Consult with MALDI-TOF manufacturer

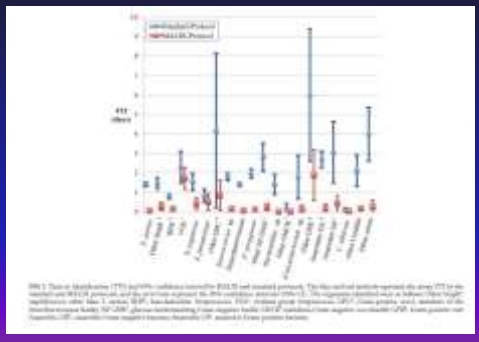
Challenges

Comment	Pre-MALDI	Post-MALDI
Microorganism Identification	Physicians familiar with current names. CLSI breakpoints	New bacterial, fungal, yeast names. No/few CLSI breakpoints. Include ID physicians and Pharmacy in on MALDI decisions
Automation of IDs	Safety steps built-in. IDs include morphology, biochemical utilization, serological tests	Safety steps need to be defined. When to accept ID? Agree with Gram stain? Treatment?
New machine, new problems	Multiple ID methods available	Multiple ID methods retired. What do you do if you do if your MALDI breaks?

Challenges

Comment	Pre-MALDI	Post-MALDI
Middleware	ID and susceptibilites can be on same instrument	MALDI **must** interface with automated susceptibility systems, LIS, etc. Who is responsible for middleware issues?
Bacterial/yeast ID	Limited IDs.	New names, susceptibilities
Blood Cultures	Culture + bottles for ID	Culture + bottles for susceptibilities ID coagulase negative Staphylococcus. What is a contaminate? Dual infections?
TAT for susceptibilities	ID and susceptibilities reported at the same time	Delay of 24-48 hours between ID and reporting susceptibility. Redo antibiograms??
Rapid Vs. MALDI IDs		MALDI for sterile sites. Use rapid IDs for urines, latex IDs, indole, colony morphology.

MALDI – Improved Time to Identification



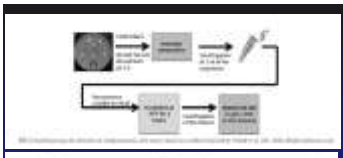
JCM 50; 3301-3308, 2012

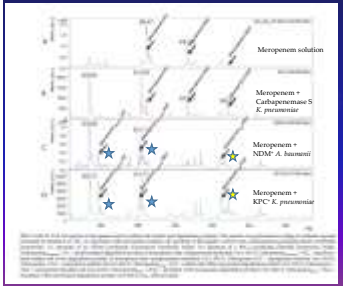
Summary (Cont.)

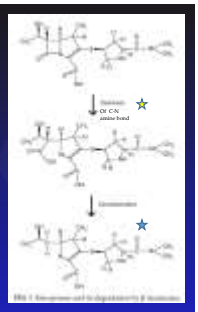
- **Problems with implementation**
  - FDA approval pending on Bruker
    - Reimbursement
      - New CPT code pending
  - Rapid ID Vs. not so rapid susceptibility testing
    - *Rapid techniques are only valuable if there is someone to act on the results*
      - Who will act on results? Do you have a plan?
        - Primary physicians, Consulting physicians, ID Pharmacists, Hospitalists?
          - Team approach
      - Real time, unit specific antibiograms
        - Helpful because IDs are available so much sooner than suscweptibilities
      - MALDI-TOF/MS susceptibilities?
        - CREs?
  - Connectivity - Middleware
    - Positive identification of microorganism throughout the workup - **Essential**
  - Acceptance by Microbiology Techs
    - Just another tool

Future Uses - Detection of Carbapenemases in the Clinical Laboratory

1. **Some β-lactamases can be inhibited by specific inhibitors**
   1. Clavulanic acid for some ESBLs
   2. Boronic acid for KPC
   3. Chelating agents for MBLs
2. **Reversal of sensitivity by production of carbapenemases**
   1. Modified Hodge test
3. **Carbapenemase detection by MALDI-TOF**
   1. Directly measure changes in M/S by hydrolysis and, in some cases, decarboxylation of the antibiotic





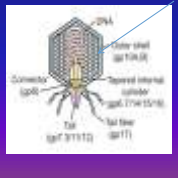


- Uses different matrix, DHB
- Different scale

CMR 26; 103-114, 2013

Bacterial Susceptibilities by Growth of Phages

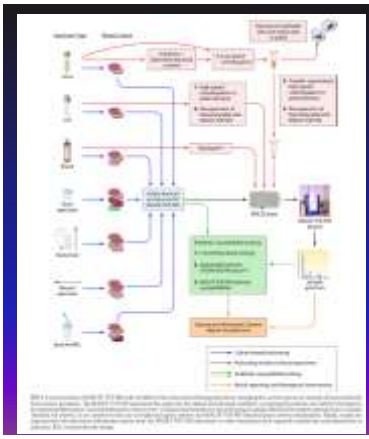
- Incubate bacteria in presence and absence of antibiotic and measure growth of bacterial phages
  - Bacterial phages require viable cells to replicate, so you will only get an increase in bacterial phages if bacteria can grow in the presence of antibiotic.
  - Bacterial phage proteins **measured** by MALDI



Detect presence of caspid proteins By MALDI-TOF

Justifications

- Reagent cost savings – JCM 2012; 3301-3308
- Return on investment (ROI) of 2-5 years. Reagent cost savings of 75% - JCM 2011;2980-2983
- Mycobacterial culture ID. Cost savings of 40:1. – JCM 2010;4481-4486
- Blood culture reduction of time to identification – JCM 2012, 3324-3328
- Cost savings associated with rapid identification of positive blood cultures - Perez KK, et al. Arch Pathol Lab Med. 2012
- Documents from bioMérieux or Bruker



Post MALDI-TOF

CMR 26;547-603, 2013

Summary

- Rapid identification ~ 1min per isolate
- Consolidation of identification testing onto a single platform
  - Current Phenotypic methods
    - Gram stain, Vitek 2, Microscan, numerous API methods, disks on media, growth characteristics, selective media, chromogenic media, biochemical tests, serologic tests, enzymatic reactions
  - Genotypic methods
    - amplified nucleic acid methods, nucleic acid sequencing
- Reduced cost per test
  - Cost will be <$1.50 per determination
- Reduced Hands-on-Time
  - Tech setup time 2-3 minutes
- Flexibility - each bench get their own target slide
- High throughput – 192 isolates/run (4 hours)
- Outbreak strain typing is possible, eventually. May need different matrix
  - Local strains can be included in a user defined database
  - Outbreaks can be identified prospectively rather than retospectively

Summary

- **MALDI-TOF/MS is faster, better, and cheaper than current full identification methods**
  - Modify to fit your laboratory.
    - Use in conjunction with rapid methods
    - RUO Vs. IVD databases
      - Amount of validation required??
  - Same identification expertise on all shifts
  - Retrospective outbreak evaluations
  - Identification directly from positive blood culture bottles and other body fluids
  - Identification not dependent on interaction with biochemicals
- **Limited reference spectra in database for some genera and species**
  - Identifications will get better
- **Can be automated**
  - Next big change in Clinical Microbiology

Summary (Cont.)

- **MALDI-TOF/MS Vs. Molecular Identification**
  - Complementary technologies
    - MALDI - requires isolated colonies or high bacterial concentrations (>10^5/mL)
    - Molecular - direct ID from patient specimens and detection of resistance genes
    - Sequencing can back-up MALDI IDs
- **It is the future**

Thank You!