International Standardization of Bed Rest Standard Measures

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Standardization of Bed Rest Studies

- International Multidisciplinary Artificial Gravity (IMAG) project (2005)
  - Standardization of AG studies
    - Screening
    - Standard conditions
    - Data management

Standardization of Bed Rest Studies

- International Countermeasures Working Group (ICMWG)
  - International Academy of Astronautics Study Group
    - International Standards for Bed Rest Studies
      - Co-Chairs: Patrik Sunblad (ESA) and Oleg Orlov (IBMP)
      - Secretary: Dave Francisco (NASA)
      - **Overall Goal:** To define and agree internationally, on standard conditions and basic, standard measurements for spaceflight related bed rest studies.
      - Standard Conditions Assessment – Oliver Angerer (ESA)
        - Meeting February 1-2, 2010 at USRA
      - Standard Measures Assessment – Ronita Cromwell (NASA)
        - Patrik Sunblad (ESA), Irina Larina (IBMP)

Standard Measures Assessment

- Identified discipline experts from each agency (NASA, ESA, IBMP) to assess the standard measures.

Discipline	ESA	NASA	IBMP
Cardiovascular	Richard Hughson	Steve Platts	Olga Vinogradova
Muscle	Joern Rittweger	Lori Ploutz-Snyder	Boris Shenkman
Bone	Joern Rittweger	Jean Sibonga	Victor Oganov
Nutrition	Petra Frings-Meuthens	Scott Smith	Irina Larina
Sensory-motor	Gilles Clement	Jacob Bloomberg	Inessa Kozlovskaya
Psychology	Elisabeth Rosnet	Walt Sipes,Kim Seaton, Steve Vanderark	Vadim Gushin
Immunology	Alexander Chouker	Brian Crucian	Marina Rykova
Hematology	Alexander Chouker	Scott Smith	Marina Rykova

Standard Measures Assessment

- Developed a list of questions to guide discussions of experts
- Collated a list of measures currently used by each agency
- Briefed experts regarding the process for telecon discussions
- Telecons are in progress; completed by the end of January
- Written reports from each discipline completed by the end of February
- A final report will be prepared and shared with all members of the IAA Bed Rest Study Group for concurrence

Clinical Laboratory Measures

ESA	NASA	IBMP
	Serum Measures	
Chemistry Profile Phosphorous, Magnesium, Glutamyltransferase, Alkaline Phosphatase, Lactate Dehydrogenase, Creatine Kinase	**Chemistry Profile** Carbon Dioxide, Blood Urea Nitrogen, Phosphorous, Magnesium, Bilirubin, Glutamyltransferase, Alkaline Phosphatase, Lactate Dehydrogenase, Creatine Kinase, Uric Acid, C Reactive Protein	**Chemistry Profile** Blood Urea Nitrogen, Phosphorous, Magnesium, Total Bilirubin, Glutamyltransferase, Alkaline Phosphatase, Lactate Dehydrogenase, Creatine Kinase, Uric Acid, C Reactive Protein
CBC/differential/platelets White Blood Count and differential, Red Blood Count, Hemoglobin, Hematocrit, Mean Corpuscular Hemoglobin (TGMH), Mean Corpuscular Hemoglobin Concentration (MCHC), Platelet Count, Reticulocyte Count	**CBC/differential/platelets** White Blood Count and differential, Red Blood Count, Hemoglobin, Hematocrit, Mean Corpuscular Volume, Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Relative (Red Cell) Distributive Width (RDW), Platelet Count, Reticulocyte Count	**CBC/differential/platelets** White Blood Count and differential, Red Blood Count, Hemoglobin, Hematocrit, Mean Corpuscular Volume, Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Relative (Red Cell) Distributive Width (RDW), Platelet Count, Reticulocyte Count
	Iron Profile Iron, Total Iron Binding Capacity (TIBC), Transferrin, Transferrin Saturation, Ferritin	**Iron Profile** Iron, Total Iron Binding Capacity (TIBC), Ferritin
	Ionized Calcium Profile Serum Ionized Calcium, pH-Serum, Ionized Calcium at pH 7.40	**Ionized Calcium Profile** Serum Ionized Calcium, pH-Serum, Ionized Calcium at pH 7.40
	Hormones Thyroxine (Free T4), Thyroid Stimulating Hormone (hTSH III)	**Hormones** Thyroxine (Free T4), Thyroid Stimulating Hormone (TSH)

Clinical Laboratory Measures

ESA	NASA	IBMP
	Urinary Measures	
Urinanalysis Specific Gravity, pH, Color, Appearance, Protein, Glucose, Bilirubin, Urobilinogen, Ketone, Nitrite, Blood, Leukocyte Esterase	**Urinanalysis** Specific Gravity, pH, Color, Appearance, Protein, Glucose, Bilirubin, Urobilinogen, Ketone, Nitrite, Blood, Leukocyte Esterase	**Urinanalysis** Specific Gravity, pH, Color, Appearance, Protein, Glucose, Bilirubin, Urobilinogen, Ketone, Nitrite, Blood, Leukocyte Esterase
	Other Creatinine	**Other** Creatinine
	Schedule for NASA Clinical Lab data collection: BR-10, BR28, BR+0, +5	

Nutrition Measures

ESA	NASA	IBMP
	Serum Measures	
Chemistry Sodium, Potassium, Chloride, Creatinine, Asparagine Aminotransferase (ASAT), Alanine Aminotrasferase (ALAT)	**Chemistry** Sodium, Potassium, Chloride, Creatinine, Aspartate Transaminase (AST), Alanine Transaminase (ALT), Cholesterol, Triglyceride	**Chemistry** Sodium, Potassium, Chloride, Creatinine, Aspartate Transaminase (AST), Alanine Transaminase (ALT), Cholesterol, Triglyceride
Clinical Blood Analysis Hemoglobin, Hematocrit, Calcium, Potassium, Sodium, Glucose	**Clinical Blood Analysis** Hemoglobin, Hematocrit, Ph, Ionized Calcium, Potassium, Sodium, Glucose	**Clinical Blood Analysis** Hemoglobin, Hematocrit, Ph, Ionized and total Calcium, Potassium, Sodium, Glucose
	Mineral Status Zinc, Selenium, Iodine, Copper, Ceruloplasmin	**Mineral Status** Zinc, Copper
	Hematologic and Iron Status Indicators Mean Corpuscular Volume (MCV), Transferrin Receptors, Transferrin, Ferritin, Ferritin Iron, Ferritin Iron % Saturation, Folate, RBC, Iron	**Hematologic and Iron Status Indicators** Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Transferrin, Ferritin, RBC, Iron, Total Iron binding capacity
	Protein Status Retinol Binding Protein, Transthyretin, Total Protein, Albumin, Alpha 1 globulin, Alpha 2 globulin, Beta globulin, Gamma globulin	**Protein Status** Total Protein, Albumin, Alpha 1 globulin, Alpha 2 globulin, Beta globulin, Gamma globulin

Nutrition Measures

ESA	NASA	IBMP
	Serum Measures	
	Hormones Testosterone, Estradiol, Dehydroepiandrosterone (DHEA), Dehydroepiandrosterone Sulfate (DHEA-S), Cortisol	**Hormones** Testosterone, Estradiol, Dehydroepiandrosterone (DHEA), Dehydroepiandrosterone Sulfate (DHEA-S), Cortisol, Free thyroxine (FT4), thyroid stimulating hormone (TSH)
	Water Soluble Vitamin Status Erythrocyte Transketolase Stimulation, Erythrocyte Glutathione Reductase Activity, Erythrocyte nicotinamide adenosine dinucleotide and nicotinamide adenosine dinucleotide phosphate (NAD/NADP), Erythrocyte Transaminase Activity, Red Cell Folate, Folate, Homocysteine, Vitamin C, Pyridoxal 5-phosphate (PLP)	
	Fat Soluble Vitamin Status Retinol, Retinyl palmitate, β-carotene, α –carotene, Serum Phylloquinone, α-tocopherol, γ-tocopherol, Tocopherol : lipid ratio, vitamin D binding protein and plasma heme	**Fat Soluble Vitamin Status** β-carotene, α –carotene, Total tocopherol
	Antioxidants and Markers of Oxidative Damage Total Antioxidant Capacity (TAC), Superoxide Dismutase (SOD), Glutathione Peroxidase (GPX), Malondialdehyde (MDA), 4-OH-alkenal, 4-hydroxynonenal, Glutathione Protein Carbonyls, Prostaglandin F2-α (PG F2-α)	**Antioxidants and Markers of Oxidative Damage** Total Antioxidant Capacity (TAC), Malondialdehyde (MDA), Prostaglandin F2-α (PG F2-α)

Nutrition Measures

ESA	NASA	IBMP
	Urinary Measures	
General pH, Creatinine	**General** Total volume, pH, Creatinine	**General** Total volume, pH, Creatinine
Minerals Calcium, Phosphorus	**Minerals** Calcium, Phosphorus, Magnesium, Copper, Selenium, Zinc, Iodine	**Minerals** Calcium, Phosphorus
	Water Sol. Vitamins N-methyl nicotinamide, 2-pyridone, 4-pyroidoxic acid	
	Protein Status 3-methyl histidine	uroproteinogramm
	Antioxidants 8-OH deoxyguanosine	
Sodium, Potassium	**Renal Stone Risk** Sodium, Potassium, Uric Acid, Citrate, Oxalate, Sulfate, Suspersaturation of Calcium Oxalate, Brushite, Struvite, Sodium, Urate, Uric Acid	**Renal Stone Risk** Sodium, Potassium, Urea, Oxalate, Uric Acid

Nutrition Measures

ESA	NASA	IBMP
Body Mass Daily	**Body Mass** Daily	**Body Mass** Daily
DXA for body composition Before and after bedrest		**DXA for body composition** Before and after bed rest
Nitrogen balance Daily (only short bedrests 5 days)		
	Schedule for NASA Nutrition Measures: BR-10, -3, BR28, BR+0, +5	***Schedule for IMBP Nutrition Measures:*** BR-30, -3, BR28, BR+0, +2.5-3.0 mo

Cardiovascular Measures

ESA	NASA	IBMP
Tilt test 30 minute Tilt + LBNP BR-2, BR+0	**Tilt test** 30 minute tilt + blood draws to measure neuroendocrine parameters BR-5, BR +0, +3	**Tilt test** Tilt at 80^0 head up for 30 minutes with blooddraws BR-5, BR +0, +3
VO2 max Cycle ergometer test BR-5, BR+2 (+0 or +1 if possible)	**VO2 max** Cycle ergometer test BR-12, -7, BR+0, +11	**VO2 max** Graded cycle exercise test BR-12, -7, BR+0, +5
	Electrocardiogram BR-5, BR7, 21, 31, BR+0, +3, +13	**Electrocardiogram** BR-5, during BR days 7,14, 21, 31, 49, 60, 75, BR+0, +3, +13, +30
	Doppler-ultrasound (2-D) BR-5, BR7, 21, 31, BR+0, +3, +13	**Doppler-ultrasound** BR-3, BR 14, 28, 42, 56, BR+0, +2
		Holter monitoring BR-4, BR 20, 30, 45, BR+0
Plasma volume BR-5, BR+0	**Plasma volume** BR-5, BR3, 21, 31, BR+0, +3	**Plasma volume** BR-5, BR +0, +3

Exercise & Muscle Measures

ESA	NASA	IBMP
Isometric maximum voluntary contraction knee, ankle, elbow 2 times pre-BR, R+0, +5		**Isometric maximum voluntary contraction:** knee, ankle, elbow
Muscle fatigue test isometric 2 times pre-BR, R+0, +5		**Muscle fatigue test isometric**
		Handgrip strength test
		Twitch interpolation
		Muscle MRI: thigh, calf, arm
	Isokinetic muscle function testing knee, ankle, trunk BR-11, -6, BR+2, +12	**Isokinetic muscle function testing** knee, ankle, trunk
	Functional fitness Muscle strength, flexibility and endurance BR-10, -5, BR+3, +13	**Functional fitness**

Bone Measures

ESA	NASA	IBMP
Urinary Bone Markers: N-telopeptide, C-telopeptide, deoxypyridinoline Pre-BR, BR20, R+0 (Daily for short-term bedrest (5 days))	**Urinary Bone Markers**: N-telopeptide, C-telopeptide, deoxypyridinoline, pyridinoline, γ-carboxy glutamic acid BR-10,-3, BR28, BR+0, +5	**Urinary Bone Markers:** N-telopeptide, C-telopeptide, deoxypyridinoline Pre-BR, BR20, R+0 (Daily for short-term bedrest (5 days))
bone alkaline phosphate and N-terminal propeptide of type I procollagen Pre-BR, BR20, R+0		bone alkaline phosphate and N-terminal propeptide of type I procollagen Pre-BR, BR20, R+0, +30
\	**Serum Bone Markers:** 25-Hydroxyvitamin D, Intact Parathyroid Hormone (PTH), Calcium, 1, 25-Dihydroxyvitamin D, Osteocalcin, Alkaline Phosphatase, Bone Specific Alkaline Phosphatase (BSAP), Serum C-telopeptide (CTX), Helical Peptide (HP), Osteoprotegerin (OPG), Osteoprotegerin ligand (receptor activator of nuclear factor-kB ligand or RANKL), Insulin-like Growth Factor, Leptin BR-10,-3, BR28, BR+0, +5	**Serum Bone Markers:** Intact Parathyroid Hormone (PTH), Calcium, Osteocalcin, Alkaline Phosphatase, Bone Specific Alkaline Phosphatase (BSAP), Serum C-telopeptide (CTX), Helical Peptide (HP), Osteoprotegerin (OPG), Osteoprotegerin ligand (receptor activator of nuclear factor-kB ligand or RANKL), Insulin-like Growth Factor, Leptin BR-10,-3, BR30, 60, BR+0, +5, +30-45
DXA whole body, hip, lumbar spine During selection, R+2 (only long-term (60 days)	**DXA** whole body, hips, lumbar spine, calcaneus, and forearm BR-13, BR+2, 6 & 12 months	**DXA** whole body, hips, lumbar spine, calcaneus, and forearm BR-13, BR+2, 6 & 12 months
pQCT radius, tibia Pre-BR, BR20, 40, 60, Post BR 2, 4 weeks, 2, 3, 6, 12 & 24 months	**QCT** Hip and lunbar spine Pre BR-3, Post BR+4, BR+365	**pQCT** radius, tibia Pre-BR, BR20, 40, 60, Post BR +5days, 4 weeks, 6, 12 months

Neurological Measures

ESA	NASA	IBMP
Motion Sickness Questionnaires motion sickness susceptibility questionnaire misery scale simulator sickness questionnaire *Used only to assess countermeasures that induce motion sickness*		
Dynamic Gait Index BR-2, R+0, R+3		
Posturography BR-2, R+0, R+3	**Functional neurological assessment** Computerized Dynamic Posturography BR-10, -4, BR+0, +1, +0, +4	
	T-reflex monosynaptic stretch reflex in primary postural muscles of the lower extremity BR-10, -4, -1, BR5, 20, 60, BR+0, +3, +5	
		Video-oculography in the tests: spontaneous activity, gaze holding, static torsional otolith-cervico-ocular reflex; oculomotor – smoothpursiut & saccades with and without retinal optokinetic stimulation (ROKS)
		Electro- oculography in the tests: eye-hand tracking with addition of biological feedback for manual tracking with and without ROKS Pre bed rest, BR1, 7, 15, 30, 40, 59, BR+0, +2, +4/5, +8/9

Psychological Measures

ESA	NASA	IBMP
Log of critical incidents When applicable	Currently assessing potential measures	**Content analysis of crew commander Daily report,** Every day during BR
Profile of mood states BR-10, -4, every 2 weeks during BR, BR+2, +10		**SAN, Modification of Luscher 8-colores test** BR-10, -4, every 2 weeks during BR, BR+2, +10
Positive and negative affect scale BR-10, -4, every 2 weeks during BR, BR+2, +10		**Spielberger anxiety test** BR-10, -4, every 2 weeks during BR, BR+2, +10
Beck depression inventory BR40		**MMPI** BR40
Sleep assessment BR-10, -4, every 2 weeks during BR, BR+2, +10		**Cognitive test battery** BR-10, -4, every 2 weeks during BR, BR+2, +10
General health questionnaire BR-10, -4, every 2 weeks during BR, BR+2, +10		**Personal self-perception and attitudes (PSPA)** BR-10, -4, every 2 weeks during BR, BR+2, +10
Device specific questions BR+1 or BR+2 for devices used during BR 1-2 days after device use if during recovery		

Immunology Measures

ESA	NASA	IBMP
	General immune status BR-10, BR28, BR+0, +5	**General immune status** (white blood cell count and differential, immunophenotype distribution, T cell function and intracellular cytokine profiles) BR-10, BR30, 60, BR+0, +5
	Viral-specific immunity BR-10, BR28, BR+0, +5	
	Latent viral reactivation BR-10, BR28, BR+0, +5	**Latent viral reactivation** (immunoglobulin antibodies to Epstein-Barr virus, EBV; viral capsid antigen, early antigen, EBV nuclear antigen and cytomegalovirus) BR-10, BR30, 60, BR+0, +5
	Physiological stress BR-10, BR28, BR+0, +5	**Physiological stress** (plasma, urinary and salivary cortisol measurements) BR-10, BR30, 60, BR+0, +5

Questions?