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ESPEN GUIDELINES

Bioelectrical impedance analysis—part II: utilization in clinical practice

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Summary BIA is easy, non-invasive, relatively inexpensive and can be performed in almost any subject because it is portable. Part II of these ESPEN guidelines reports results for fat-free mass (FFM), body fat (BF), body cell mass (BCM), total body water (TBW), extracellular water (ECW) and intracellular water (ICW) from various studies in healthy and ill subjects. The data suggests that BIA works well in healthy subjects and in patients with stable water and electrolytes balance with a validated BIA equation that is appropriate with regard to age, sex and race. Clinical use of BIA in

Abbreviations: BCM, Body cell mass; BF, Body fat; BIA, Bioelectrical impedance analysis; BIS, Bioelectrical impedance spectroscopy; BMI, Body mass index; BIVA, Bioelectrical impedance vector analysis; DXA, Dual-energy X-ray absorptiometry; ECW, Extracellular water; FFM, Fat-free mass; ICW, Intracellular water; MF-BIA, Multi-frequency bioelectrical impedance analysis; PhA, Phase angle; *R*, Resistance; SF-BIA, Single frequency bioelectrical impedance analysis; TBK, Total body potassium; TBW, Total body water; Xc, Reactance.

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Total body water;
Extracellular water;
Intracellular water;
Body cell mass

subjects at extremes of BMI ranges or with abnormal hydration cannot be recommended for routine assessment of patients until further validation has proven for BIA algorithm to be accurate in such conditions. Multi-frequency- and segmental-BIA may have advantages over single-frequency BIA in these conditions, but further validation is necessary. Longitudinal follow-up of body composition by BIA is possible in subjects with BMI 16–34 kg/m^2 without abnormal hydration, but must be interpreted with caution. Further validation of BIA is necessary to understand the mechanisms for the changes observed in acute illness, altered fat/lean mass ratios, extreme heights and body shape abnormalities.

Background

Nearly 1600 papers about BIA are found in English medical literature between 1990 and 2003, with 450 being published in the last 3 years. This vast body of literature makes it difficult to understand when and how BIA should be used. Part I of these ESPEN 2-part guidelines on BIA discussed the principles, methods and BIA equations.[1]

Part II of these guidelines, limited to adults, reviews the current applications and limitations and presents the ESPEN recommendations for BIA in clinical practice as follows:

(a) BIA measurement conditions.
(b) Healthy subjects, ethnic groups and body shape abnormalities.
(c) Conditions with a potential for weight loss or being underweight.
(d) Conditions of overweight or obesity.
(e) Conditions of altered hydration.

This review does not cover BIA measurements in children. Interpretation of BIA is difficult in children, because of variations in body composition due to interindividual differences in growth velocity and puberty related changes.

BIA measurement conditions

The factors/conditions that affect BIA are shown in Table 1. Subjects must be measured (recall values are not acceptable) for height and weight at the time of the BIA measurement. Standardized conditions with regard to body position, previous exercise, dietary intake and skin temperature must be respected.[2–4] Consumption of food and beverage may decrease impedance by 4–15 Ω over a 2–4 h period after meals, representing an error smaller than 3%.[2,4] Measurements on two consecutive days at the same time in the nourished state were highly reproducible ($4 \pm 20\,\Omega$, non-significant) in patients with stable chronic obstructive pulmonary disease. BIA results are most affected by whether subjects was in a fasting or a fed state.[5] Compared to baseline, exercise was shown to decrease *R* by ≈3% and Xc by ≈8% immediately post-exercise, with measurements returning to normal when repeated 1 h later.[6] A 3% increase in *R* (17 Ω) was observed after 60 min of recumbence.[7] Errors of ≈1.0–1.5 l in predicted TBW may occur in individuals who are restricted to bed rest for several hours or days when BIA equations are used that were developed in subjects who were measured within 5 min after subjects were lying down. Greater errors can be expected for ECW because this compartment is more dependent on gravitational shifts. This is reflected by a greater shift in *R* at low frequencies of measurements. No interference with pacemaker or defibrillators is anticipated.[6] Although there are no known incidents reported as a result of BIA measurements, the possibility cannot be eliminated that the induced field of current during the measurement could alter the pacemaker or defibrillator activity. Therefore the patient should be monitored for cardiac activity.

Conclusion: Standardized methodology (Table 1) must be observed to optimize measurements. Universally standardized protocols of BIA measurements have to be developed and implemented.

Healthy subjects, ethnic groups and body shape abnormalities

It is essential that appropriate BIA equations are chosen for the population studies. Published

Table 1 Recommendations for clinical application of bioelectrical impedance analysis*

	Definition/comments	Recommendations
Instruments/material		
Generator	Consistent signal of reproducible amplitude	Calibration of electrical equipment
	Batteries	Battery-powered to avoid interference with current variations
		Autonomy for >20 measurements
Analyzer	Measures *R* or impedance and Xc or phase angle	Regular calibration against known ohmmeter
		Identify type of signal measured (i.e. impedance or *R* or PhA or Xc)
	Automatic verification of skin resistance	Identify abnormal skin resistance, in cases of excessive resistance (e.g. pachydermia)
Cables	Length	Appropriate for length of subject height (up to 2 m)
	Diameter/isolation	Meets manufacturer's recommendation
Electrodes	Surface size	Meets instrument requirements ($>4\,cm^2$)
	Integrity of gel	Keep electrodes in sealed bag. Protect against heat
Statiometer	Calibrated to 0.5 cm	Use tape measure for subjects who are unable to stand and for knee-ankle height or arm span
Scale	Calibrated to 0.1 kg	Regular cross-calibration with other scales
Subjects		
Height Weight	Measure height (0.5 cm) and weight (0.1 kg) at the time of the BIA measurement	Self-reported height and weight are not valid
Food, drink, alcohol	Fasting/no alcohol for >8 h recommended	Shorter periods of fasting may be acceptable for clinical practice (versus research)
Bladder voided		Subject has voided before measurement
Physical exercise		No exercise for >8 h
Timing	Note time of measurement	For longitudinal follow-up, perform measurement at the same time of day
		Note menstrual cycle
Skin condition	Temperature	Ambient temperature
	Integrity	No skin lesions at the sight of electrodes. Change site of electrodes
	Cleaning	Clean with alcohol
Electrode position	Note body side of measurement	Always measure same body side
	Distance between electrodes	Minimum of 5 cm between electrodes. If needed, move proximal electrode
Limb position	Abduction of limbs	Arms separated from trunk by about 30° and legs separated by about 45°
Body position	Supine, except for "scale" type BIA instruments	Ambulatory subjects supine for 5–10 min. For research protocol, standardize time that subjects are

Table 1 (*continued*)

	Definition/comments	Recommendations
		supine before measurement. Note if subject is confined to bed (patients)
Environment	Electrical interference	No contact with metal frame of bed. Neutral environment (no strong electrical or magnetic fields)
Body shape	Note body abnormalities	Note measurement validity (e.g. *R* or Xc outside of expected range for subject). Consider validity of measurement when interpreting results (e.g. abnormally low *R* suggests edema)
	Amputation	Measure non-affected limb. Not valid for research, but permits determination of body compartment, because measurement error is consistent
	Atrophy, hemiplegia	Measure non-affected side. See Table 6 for limitations
	Abnormal limb or trunk (e.g. scoliosis)	Note abnormal condition
	Dystrophy (HIV, Cushing's syndrome etc.)	Limited validity in conditions of abnormal body compartment distribution
	Obesity	Use electricity-isolating material (e.g. towel) between arm and trunk, and between thighs
Ethnic group		Note race. Use race-specific BIA equation, if applicable
*Disease conditions**		
Cardiac insufficiency	Edema interferes with measurement	Measure patient in stable condition
Liver failure	Ascites/edema interferes with measurement accuracy	Consider segmental BIA measurement
Kidney failure	Edema/altered ion balance interferes with measurement	
Abnormal serum electrolyte concentrations	Electrolyte concentration affects BIA measurement	Perform BIA when serum electrolytes are within normal range. Compare BIA results when serum electrolyte concentrations are similar
Hypothyroid	Pachydermia	May invalidate measurement because of high skin resistance
*Treatments**		
IV/Electrolyte infusions	Peripheral edema interferes with measurement	Measurements are invalid if patient is abnormally hydrated
Drugs that affect water balance	Steroids, growth hormone, diurectics	If patient is in stable condition, measurement should be effected at the same time after medication administration
Dialysis	Hemo-, peritoneal dialysis	Use special protocols, standardize measurement procedure, i.e. measurement should be performed 20–30 min post-dialysis
Ascites puncture		Use special protocols, standardize measurement procedure

Table 1 (*continued*)

	Definition/comments	Recommendations
Orthopedic prosthesis/implants (metal)	E.g. hip prothesis	Measure non-affected body side. Note prosthesis/implants
Pacemakers Defibrillators	Implanted cardiac defibrillator	No interference with pacemakers or defibrillators is anticipated.[6] Although there are no known incidents reported as a result of BIA measurements, the possibility cannot be eliminated that the induced field of current during the measurement could alter the pacemaker or defibrillator activity. Therefore, the patient should be monitored for cardiac activity

*See Table 6 for further discussion.

equations and criteria of selection are presented in part 1. Longitudinal changes in FFM and BF can be assessed with BIA, but are controversial when significant weight loss occurs because of physiological changes.[8–13] Assessment of changes in FFM, BF or TBW of less than 1.5–2 kg is limited, because of limitations in BIA precision.[14] Reproducibility over a 7-week period was excellent in weight stable subjects.[15] Longitudinal changes in FFM or BF must be interpreted with caution in the presence of altered hydration.[16,17]

The use of general prediction equations across ethnic populations without prior testing of their validity should be avoided, because of existing differences in body build among ethnic groups.[18,19] Failing to adjust for differences in FFM hydration fraction in ethnic groups may result in systematic biases.[19]

The inhomogeneous nature of the various body compartments and large variations in cross-sectional areas are likely responsible for the lack of portability of BIA equations from one population to another, such as from young to elderly subjects, or from normal weight to obese or severely underweight subjects. In addition, differences in conductor lengths from limbs and trunk are likely to be responsible for the lack of portability of BIA equations between ethnic groups. In this context, Heitmann et al.[20] previously showed that variations between *R* and height, most likely due to the different relative sitting heights, influence BIA results. This might support the use of segmental BIA (trunk or limb BIA), which overcomes differences in distribution of body compartments between limb and trunk. However, the distribution of body water between the intra- and extracellular space is also partly responsible for population specificity of prediction equations (e.g. age or sex effects, pregnancy).

Conclusions: In addition to methodological limitations mentioned in Table 1, we draw the following conclusions:

- Healthy adults: BIA equation has to be validated in the population studied (e.g. race, age, sex-specific).
- Healthy elderly: A number of BIA equations developed in young subjects result in large bias in older subjects. Population-specific equations or equations that adjust for FFM and BF changes with age are recommended.
- Ethnic groups: The use of BIA equations has to be adapted to the ethnic group studied.
- Longitudinal changes: FFM and BF changes can be assessed by BIA in subjects without abnormal hydration, but must be interpreted with caution and are limited by BIA precision.
- Body shape abnormalities, very small or large body heights or relative sitting heights: The use of general prediction equations in subjects with abnormal body build, e.g. acromegaly or amputation, should be interpreted with caution. Use of segmental BIA requires further validation in such conditions.

Future developments:

- BIA equations and reference values should be developed for ethnic groups.
- The validity of segmental BIA in subjects with body shape abnormalities or extreme body height is to be determined.

Conditions in specific groups with an emphasis on those at risk for malnutrition and weight loss

Table 2 shows that variable and contradictory results are obtained by BIA for FFM, BF and BCM in various pathologies[15–17,21–33] by a number of different BIA equations[22,27,29,30,34–49] with comments or evaluation shown in the last two column of the table. These discrepancies stem not only from the BIA method limitations but also from limitations in reference methods (see part I).[1]

Abnormal tissue conductivity may also be responsible for the inadequacy of BIA equations developed in healthy subjects when applied to patients with lean tissue abnormalities, such as neurological disorders.[50] Potential sources of errors for BIA in subjects with acromegaly syndrome may be due to increased bone mass of limbs and changes in skin thickness and hydration, which might influence the extension of the tissues electrical characteristics.[32] In patients with moderate fluid overload, such as cirrhotic patients without ascites, changes in electrical conductivity of the lean tissue might be less marked in the arms than in the legs.[32] This might explain the advantage of segmental BIA (trunk or limb BIA).[51]

A greater variability of ECW:ICW ratio may be responsible for the lower accuracy of BIA and the greater contribution of weight to the unexplained variance of total FFM and FFM_{leg} in anorexia nervosa[33] and cachexia. An altered ICW to ECW distribution is suggested by low phase angle.[52] Thus, SF-BIA body composition parameters must be interpreted with caution in early refeeding in anorexia nervosa and cachectic subjects who might have altered tissue hydration.[53]

Studies using raw BIA data, i.e. phase angle (PhA), are shown in Table 3. PhA has been correlated with the disease prognosis in HIV-infection,[54,55] hemodialysis,[56] peritoneal dialysis,[57] chronic renal failure[58] and liver cirrhosis patients.[59] These studies suggest that PhA may be useful in determining increased risk of morbidity and that PhA decreases with age.

Studies using the BIVA are shown in Table 4.[60–68] Abnormal body composition was detected by BIVA in renal insufficiency,[66] dialysis,[67] liver disease,[68] lung cancer patients[64] and patients with other cancers.[65] The BIVA in the elderly showed a clear trend for a reduction of FFM with age, with the greatest changes occurring after 80 y.[62] BIVA requires further validation.

Conclusions: Based on these studies in Tables 2–4, we draw the following conclusions:

- Severely malnourished and anorexia nervosa patients (BMI $<16\,kg/m^2$): BIA results are affected by variable tissue hydration and should be interpreted with caution during early refeeding.
- In patients with extremes BMI (<16 or $>34\,kg/m^2$), prediction errors appear to be important, but it is possible to obtain estimates of longitudinal changes in FFM and BF with weight gain or loss in subjects with BMIs of 16.0–34 kg/m^2.
- Abnormal tissue hydration, edema: Inter-individual differences of lean tissue hydration are probably too high to develop uniform equations to assess FFM, BF or BCM and thus the application of whole-body, SF-BIA is not appropriate in these circumstances.
- Neuromuscular diseases (e.g. Duchenne muscular dystrophy, post-traumatic paraplegia/hemiplegia): use of BIA equations requires further validation. Use of segmental BIA may be recommended in these conditions for long-term follow-up.
- Segmental-BIA appears to be able to detect abnormalities in patients with altered body geometry and may detect altered fluid status.
- Phase angle: Low PhAs have been shown to be of prognostic relevance in HIV-infected, peritoneal and hemodialysis, liver disease patients and elderly subjects.
- BIVA method is able to detect altered tissue electrical properties in ill subjects and may be more predictive of prognosis than weight loss, but this method is limited, because it does not give any indication of FFM and BF reserves.

Future developments:

- Further validation of segmental-BIA in subjects with altered body geometry, fluid status and fat distribution is necessary.
- Confirmation of the relevance of low PhA in the prediction of survival in larger populations is necessary.
- Confirmation of altered tissue electrical properties by BIVA in the prediction of disease prognosis in larger populations is necessary.

Conditions of overweight and obesity

The studies[69–74] that have evaluated BIA in overweight and obese subjects are shown in Table 5, with comments or evaluation shown in the last column of the table. Currently, it appears that BIA

Table 2 BIA studies evaluating FFM, BF and BCM in specific groups of subjects and with an emphasis on those at risk of malnutrition

Author	Subject group	*n*	BIA parameter	Reference	Method/ equation used	Instrument	Mean bias ± SD or 95%CI[a]	*r*	SEE	Comments/ appreciation	Study type; Limitations (L)
Bosaeus et al.[16]	GH deficient subjects	23	BF	DXA -L	Manufacturer	RJL	−3.5; −5.0; −2.0	0.88	3.5	At baseline, large underestimation of BF. Population specific equation might improve results	*A*; longitudinal study; L: small sample size
	GH longitudinal follow-up	22	BF	DXA -L	Manufacturer	RJL	1.23; −0.03; −2.5	0.55	2.8	At follow-up, lower correlations between methods, with overestimation of BF loss	
Beshyah et al.[17]	GH deficient subjects	43	FFM	DXA -L	Lukaski et al.,[34] Kushner and Schoeller[35]	Holtain	0.8	0.93		DXA- and BIA-derived FFM highly correlated. Use of BIA is questioned in clinical situations associated with TBW Δ	*A*; longitudinal study
Smith et al.[21]	Cancer	38	%BF	DXA-H	Segal et al.[36]	RJL	4.2 ± 4.1			Large errors between BIA and reference methods for % BF were noted in prostate cancer with geriatric equation	*B*
					Deurenberg et al.[37]		−11.4 ± 4.9				
Kotler et al.[22]	HIV	134	FFM	DXA -L	Kotler et al.[22]	RJL		0.9	4.80%	Disease (HIV) did not affect the prediction	*B*
			BCM	TBK				0.89	10.20%		
Corcoran et al.[23]	AIDS wasting	132	FFM	DXA-H	Manufacturer	RJL	−1.5 ± 2.9	0.92		Lukaski and Bolonchuk and Segal equations resulted in minimal bias in lean subjects. BIA significantly different from DXA with other equations. BIA overestimated FFM in those with greater BF	*B*
					Lukaski et al.[34]		1.5 ± 2.9	0.94			
					Lukaski and Bolonchuk[38]		0.7 ± 2.8	0.94			
					Kotler et al.[22]		−1.4 ± 3.2	0.90			
					Deurenberg et al.[39]		2.4 ± 2.6	0.94			
					Segal et al.[36]		1.0 ± 2.6	0.94			
					Van Loan and Mayclin[40]		−6.2 ± 4.1	0.86			
					Gray et al.[41]		1.3 ± 3.3	0.93			
Steiner et al.[15]	COPD	85	FFM	DXA -L	Schols et al.[42]	Bodystat	0.72; −5.7; 7.2	0.51		BIA overestimated FFM. Mean differences were small, but limits of agreement relatively large. Reproducibility over a 7-week period was excellent	*B*
Kyle et al.[24]	Heart, lung and liver transplant patients	245	FFM	DXA-H	Kyle et al.[43]	Xitron	0.3 ± 2.3	0.97	2.3	BIA permits estimation of FFM in pre- and post-transplant patients	*B*

Nau et al.[25]	Amyotrophic lateral sclerosis	23	FFM	DXA –L	Segal et al.[45]	RJL	−0.95	0.88	3.2	Non-significant difference between DXA and BIA for the two equations	*B*; L: small sample size
					Lukaski et al.[34]	RJL	0.24	0.93	3.3		
Desport et al.[26]	ALS	32	FFM	DXA –L	Various equations[34,40,41]	Analycor3	0.7±5.1%			Suggests need for populations-specific BIA equations	*B*; L: small sample size
Roubenoff et al.[27]	Elderly, Framingham study	161 M	FFM	DXA –L	Roubenoff et al.[27]	RJL	0.0	0.85	3.4	Lukaski equation, derived in thinner/ younger subjects, underestimated FFM in the older/heavier Framingham cohort. The Roubenoff equation, derived in the Framingham subjects, overestimated FFM in taller/less obese New Mexico Study subjects. Differences in DXA instruments (same manufacturer) may have contributed to result differences	*B*
		294 F			Roubenoff et al.[27]		0.0	0.88	2.1		
		161 M			Lukaski et al.[34]		−2.13	0.85	4.0		
		294 F			Lukaski et al.[34]		−2.64	0.88	2.7		
	Elderly, New Mexico	116 M			Roubenoff et al.[27]		2.5	0.87	2.3		
		167 F			Roubenoff et al.[27]		2.5	0.86	1.6		
		116 M			Lukaski et al.[34]		0.47	0.87	3.2		
		167 F			Lukaski et al.[34]		0.12	0.85	2.2		
Genton et al.[28]	Elderly	100 M	FFM	DXA-H	Deurenberg et al.[37]	Xitron	−6.7±2.7	0.87	2.6	Deurenberg and Roubenoff equations underestimate and Baumgartner overestimated FFM. Geneva equations accurately predicted FFM in Swiss elderly subjects	*B*
					Baumgartner et al.[46]		1.4±2.5	0.88	2.4		
					Roubenoff et al.[27]		−2.3±2.1	0.94	1.7		
					Kyle et al.[43]		0.2±2.0	0.94	2.0		
		106 F	FFM	DXA-H	Deurenberg et al.[37]	Xitron	−7.1±2.3	0.89	2.0		
					Baumgartner et al.[46]		4.3±2.9	0.91	2.8		
					Roubenoff et al.[27]		−2.9±1.7	0.94	1.2		
					Kyle et al.[43]		0.0±1.6	0.89	1.6		
Haapala et al.[29]	Elderly women	93	FFM	DXA -L	Manufacturer	RJL	5.5±2.7; 0.1;10.9			BIA prediction equations must be chosen with care	*B*; L: BIA and DXA measurements not performed at the same time
					Segal et al.[45]		0.3±2.0; −3.7; 4.3				
					Deurenberg et al.[37]		−6.5±2.4; −11.3; −1.7				
					Heitmann[47]		0.4±1.9; −3.4;4.2				
					Swendsen et al.[48]		2.3±3.2; −4.1; 8.7				
					Roubenoff et al.[27]		−2.0±2.0; −6.0;2.0				
					Piers et al.[49]		−0.8±2.4; −5.6; 4.0				
					Kyle et al.[43]		1.3±2.5; −3.7; 6.3				
					Haapala et al.[29]		−0.5±1.6; −3.7; 2.7				

Table 2 (*Continued*)

Author	Subject group	*n*	BIA parameter	Reference	Method/ equation used	Instrument	Mean bias ± SD or 95%CI	*r*	SEE	Comments/ appreciation	Study type; Limitations (L)
Dey and Bosaeus[30]	Elderly	106	FFM	4 comp	Roubenoff et al.[27]	RJL	3.4; −2.2; 9.0	0.95	2.8	BIA equations need to be developed and validated in the population under study	*B*
					Deurenberg et al.[37]		8.5; 2.8; 14.2	0.95	2.9		
					Kyle et al.[43]		0.6; −5.4; 6.7	0.94	3.1		
					Dey and Bosaeus[30]		−0.01; −5.2; 5.2	0.95	2.5		
Pirlich et al.[31]	Cushing syndrome	15	BCM	TBK	see reference	Data input	3.9 ± 3.2	0.85		BIA overestimated BCM by 18%. Limits of agreement between methods were large	*B*; L: small sample size
Pirlich et al.[32]	Cirrhosis w/o ascites	17	BCM	TBK	Kotler et al.[22]	Data input		0.95	2.3	Inclusion of segmental impedance data in patients improved the predictive power of final BIA	*B*; L: small sample size
	with ascites	16	BCM	TBK	Kotler et al.[22]			0.66	2.5		
	Cushing's	12	BCM	TBK	Kotler et al.[22]			0.84	3.0		
	Acromegaly	18	BCM	TBK	Kotler et al.[22]			0.95	2.3		
Pirlich et al.[32]	Cushing syndrome	12	BCM	TBK	Segmental using arm	Data input		0.96	1.6	Segmental BIA improved assessment of BCM in malnourished and patients with acromegaly, but not in patients with fluid overload	*B*; L: small sample size
	Acromegaly	18	BCM	TBK	Segmental using trunk			0.97	2.1		
Bedogni et al.[33]	Anorexia Nervosa	35	FFM	DXA -L	SF-BIA and segmental	RJL		0.88	1.9 (5%)[b]	Population-specific BIA equations gave good estimates of total and appendicular FFM in anorexics, with higher prediction error in anorexics than controls. Lower BIA accuracy may be due to greater ECW:ICW ratio variability	*B*
			FFM_{leg}	DXA -L		RJL		0.87	0.5 (7%)[b]		

FFM, fat-free mass; BF, body fat; BCM, body cell mass; DXA, dual energy X-ray absortiometry; DXA-L, Lunar; DXA-H, Hologic; DXA-N, Norland; TBK, total body potassium; GH, growth hormone; COPD, chronic obstructive pulmonary disease.

Data Input, Hofheim, Germany; RJL Systems, Inc, Clinton Twp, MI, USA; Xitron Technologies, San Diego, CA; Human-IM Scanner, Dietosystem, Milan, Italy; Analycor3, Spengler, France; Valhalla Scientific, San Diego, CA, USA; Holtain, Holtain Ltd, Crosswell, United Kingdom; BodyStat, Bodystat Ltd, Douglas, UK.

A: randomized, controlled clinical trial; *B*: controlled clinical trial, non-randomized; *C*: non-controlled prospective clinical trial; *D*: controlled study of case studies with weak methodology; *R*: review article.

[a]95% confidence interval.

[b]RSME=root square mean error.

Table 3 BIA studies showing an association between Phase Angle (PhA) and survival

Author	Subject group	*n*	BIA parameter	Instrument	Comments/ appreciation	Study type; Limitations (L)
Ott et al.[54]	HIV	75	PhA	RJL	PhA $>5.6^{\circ}$ was a significant predictor ($p<0.001$) of survival in HIV-infected patients	*B*
Schwenk et al.[55]	HIV	469	PhA	Data input	Low PhA ($<5.3^{\circ}$) remained an independent prognostic marker of clinical progression and survival. Survival was shorter in patients with PhA $<5.3^{\circ}$ (463 d; 397, 528) compared to patients with PhA $>5.3^{\circ}$ (697 d; 690, 705)	*B*
Maggiore et al.[56]	Hemodialysis	131	PhA	RJL	Patients with PhA in lowest quartile (men $<4.5^{\circ}$, women $<4.2^{\circ}$) had significantly lower 2-y survival (51.3% versus 91.3%)	*B*
Fein et al.[57]	Peritoneal dialysis	45	PhA	RJL	Peritoneal dialysis patients with a PhA $>6.00^{\circ}$ had significantly longer survival (p=0.01)	*B*
Bellizzi et al.[58]	Chronic renal failure	46	PhA	RJL	Decline in PhA was associated with reduced survival, even when biochemical markers were unchanged. Mortality was 28% in patients with PhA $<3.0^{\circ}$ versus 3% with PhA $>3^{\circ}$	*C*; L: abstract only
Selberg and Selberg[59]	Cirrhosis	305	PhA	RJL	Patients with PhA $<5.4^{\circ}$ had significant ($p<0.01$) shorter survival	*B*

BIA-2000-M, Data Input, Hofheim, Germany; RJL Systems, Inc, Clinton Twp, MI, USA.
A: randomized, controlled clinical trial; *B*: controlled clinical trial, non-randomized; *C*: non-controlled prospective clinical trial; *D*: controlled study of case studies with weak methodology; *R*: review article.

equations can estimate body composition in overweight patients. BIA has been shown to be valid with BMIs to 34 kg/m^2.[24,43] In morbid obesity, most predictive equations are unable to predict static body composition and are not reproducible for individuals over time.[69] The disproportion between body mass and body conductivity lowers the accuracy of BIA in obesity. The trunk contributes about 50% of conductive mass, but only about 10% of total body impedance.[75–77] Despite of enhancements in BIS technology, the differentiation of ICW and ECW in obesity remains elusive.[78]

Empirical regression models are of limited value and very population-specific because of interference effects (abnormal hydration, increased fat fraction, abnormal geometric tissue distribution, etc.) across various body segments in different populations, but especially in obese subjects.[79]

Table 4 BIA studies showing changes in body composition by bioelectrical impedance vector analysis (BIVA) vector graph

Author	Subject group	*n*	Comments/appreciation	Study type Limitations (L)
Piccoli et al.[60]	Obesity	540	Edema could be identify in 91% of obese subjects with impedance vectors. A different impedance vector pattern was associated with weight loss in obesity due to fluid removal versus an energy-restricted diet	*B*
Guida et al.[61]	Obesity	516	BMI influenced the impedance vector distribution pattern, which proved to be consistent up to a BMI of 65 kg/m^2. Obese women with an altered body composition can be identified and monitored using vector BIA	*B*
Buffa et al.[62]	Elderly	201	Lean body mass reductions were noted with age, with the greatest changes occurring after age 80 y. BIA parameters approached values typical of pathological lean subjects (cachexia and anorexia)	*B*
Cox-Reijven et al.[63]	Gastrointestinal disease	70	Low sensitivity, but high specificity of vector BIA in detecting depletion in gastrointestinal patients. Further validation seems necessary	*B*; L: used published data for control group, not the same population
Toso et al.[64]	Lung cancer	63	Altered body composition in lung	*B*
Toso et al.[65]	Cancer of mixed origin	92	cancer and cancer patients of mixed origin, as reflected by reduced Xc and preserved *R* values	*B*
Piccoli et al.[66]	Chronic renal failure	91	Vectors from patients with edema were displaced downward on the *R* Xc graph, compared to the healthy population	*B*
Piccoli and Italian CAPD BIA study group[67]	Peritoneal dialysis	200	Vectors from patients with edema were displaced downward on the *R* Xc graph (88% sensitivity, 87% specificity), and were close to vectors from nephrotic patients. Whether CAPD patients with vector within the target ellipse have better outcome needs longitudinal evaluation	*B*
Guglielmi et al.[68]	Cirrhosis	305	All liver cirrhosis patients with clinically detectable edema fell outside the 50% tolerance ellipse for the healthy subjects. The abnormalities were proportional to the stage of liver failure and the degree of fluid imbalance. BVIA can detect fluid imbalances, but cannot quantify fluid volume	*B*

Comment: All studies used RJL instruments by RJL Systems, Inc, Clinton Twp, MI, USA
A: randomized, controlled clinical trial; *B*: controlled clinical trial, non-randomized; *C*: non-controlled prospective clinical trial; *D*: controlled study of case studies with weak methodology.

Scharfetter et al.[80] proposed a localized fat estimation procedure which measures a well-defined abdominal segments and found highly linear correlations between subcutaneous fat layer thickness and SF-BIA across the waist. This method may permit to assess abdominal obesity, but

Table 5 Bioelectrical impedance analysis (BIA) studies in overweight and obese subjects

Author	Subject group	*n*	BIA parameter	Reference	Method/ equation used	Instrument	Mean bias ± SD or 95%CI	*r*	SEE	Comments/appreciation	Study type; Limitations (L)
Hendel et al.[69]	Obese	16	FFM	DXA-N	SF-BIA, various equations	Animeter				In obesity, most predictive equations are unable to predict static body composition and are not reproducible for individuals over time. However, a significant or insignificant change in *R* may be used to indicate whether FFM is lost or preserved in groups of obese subjects	*B;* L: small sample size
Das et al.[70]	Extremely obese	20	%BF	3 comp	Manufacturer	RJL	5.7 ± 0.6; 0.6; 10.8*			Lukaski equation provided mean % BF values closest to reference method in extremely obese, weight-reduced state and for changes over time. The %BF limits of agreement were much broader than with other body composition methods, making BIA a method more suitable for population groups than for individuals	*B*; L: small sample size
					Lukaski et al.[34]		1.1 ± 0.7; −4.7; 6.9*				
					Segal et al.[36]		1.5 ± 0.5; −2.8;5.9*				
	Weight reduced				Manufacturer	RJL	5.1 ± 1.1; −4.8; 14.9*				
					Lukaski et al.[34]		0.4 ± 1.2; −10.6; 11.4*				
					Segal et al.[36]		−4.8 ± 1.2; −15.4;5.8*				
Tagliabue et al.[71]	Obese	68	Arm FFM	DXA –L	MF-BIA	Human-IM		0.93	0.8	Better prediction of FFM in obese with segmental BIA (low frequencies for the arm and high frequencies for the leg)	*B*
	Obese	68	Leg FFM	DXA –L	MF-BIA	Human-IM		0.93	1.5		
Cox-Reijven and Soeters[72]	Obese	90	TBW	^2H_2O	BIS-Hanai	Xitron	0.3; −3.9; 4.5	0.95		BIS, with obesity specific constants, was slightly more accurate in obese subjects than linear regression, but was not sensitive enough for clinical use	*B;* cross-validation
	Obese	90	ECW	NaBr	BIS	Xitron	0.8; −2.6; 4.2	0.86			
Cox-Reijven et al.[73]	Obese	10	ΔTBW	^2H_2O	BIS-Hanai	Xitron	−2.4; −8.1; 3.4	0.69		BIS overestimated fluid loss during weight loss in morbidly obese subjects. The higher the % BF of the weight loss, the more BIS overestimated the loss of TBW	*B;* longitudinal; L: small sample size
	Obese	10	ΔECW	NaBr	BIS-Hanai	Xitron	0.7; −5.3; 3.9	0.54			
De Lorenzo et al.[74]	Obese	55	TBW	^2H_2O	MF-BIA	Xitron	0.1; −5.4; 5.5	0.94	2.8	MF-BIA to determine TBW included body volume and impedance at 2 frequencies (1 and 100 kHz)	*B*

FFM, fat-free mass; TBW, total body water; BF, body fat; DXA, dual energy X-ray absortiometry; ^2H_2O, deuterium oxide; NaBr, sodium bromide; MF-BIA, multifrequency BIA; BIS, bioelectrical impedance spectroscopy; DXA-L, Lunar, Lunar Radiation Corp, Madison, WI, USA; DXA-N, Norland, Norland Medical Systems, Fort Atkinson, WI, USA; SD, standard deviation; SEE, standard error of the estimate.

Animeter, Odense, Denmark; RJL Systems, Inc, Clinton Twp, MI, USA; Human-IM Scanner, Dietosystem, Milan, Italy; Xitron Technologies, San Diego, CA, USA.

A: randomized, controlled clinical trial; *B*: controlled clinical trial, non-randomized; *C*: non-controlled prospective clinical trial; *D*: controlled study of case studies with weak methodology.

*Limits of agreement.

requires further investigation to determine its clinical application.

Conclusions: Based on these studies in Table 5, we draw the following conclusions:

- Initial measurement: BIA results are valid up to 34 kg/m^2, but must be interpreted with caution in subjects with BMI $>$ 34 kg/m^2 and requires further validation in these subjects.
- Longitudinal follow-up: Although the error in absolute values of FFM and BF are greater at extremes of body weight, it is possible to obtain estimates of longitudinal changes in FFM and BF with weight gain or loss in moderately obese subjects, subject to limitations in BIA precision (1.5–2.0 kg).
- Segmental-BIA (trunk) and localized BIA (arm, thigh or abdominal section) may be able to evaluate BF in obese subjects, but further validation is required.

Future development: Further validation of BIA, including segmental- and localized BIA, is necessary in obese and morbidly obese subjects.

Conditions with a potential for altered hydration

Table 6 shows various studies[81–118] in subjects with altered hydration, which determine TBW, ECW and BCM based on a number of body composition models or equations,[22,35,38,40,45,119–125] with comments or evaluation shown in the last two columns of the table. These discrepancies stem not only from the BIA method limitations but also from limitations in reference methods (see part I).[1]

In a short-term within-subjects experiment, Gudivaka et al.[82] found an accuracy of 0–200 ml and a precision of 500–800 ml with the Cole–Cole model when the effects of other biological parameters (orthostatic changes, conductivity of body tissue, etc.) that influence impedance independent of volume were eliminated.

MF-BIA correlated well with changes in weight and body fluid compartments in patients going from overhydration to euvolemia, but did not correlate with these changes in patients going from dehydration to euvolemia.[85] This suggests that MF-BIA is limited in its ability to quantify the magnitude of fluid volumes over time. Confounding effects, such as simultaneous changes in electrolyte concentration, changes in cylinder (leg) diameter and skin temperature in addition to changes in impedance, may be in part responsible for the inability to measure changes in hydration.[79] Furthermore, it is necessary to demonstrate that the results are not influenced by changes in specific conductivity (muscle, blood, etc.) or orthostatic effects.[3]

Differences noted between dilution (bromide, deuterium) and BIA methods (MF-BIA and BIS) are largely due to errors because BIA does not measure the body compartments directly, and errors are likely due to the inhomogeneous nature of the various body compartments and the large variations in cross-sectional area between, for example, thigh versus trunk.[110] BIA is limited because large changes in the volume of the trunk may result in relatively small changes in total body *R*. The errors found limit the clinical usefulness of the MF-BIA and BIS methods for the assessment of ECW and TBW in individual patients. In patients with severe fluid overload, inter-individual differences of lean tissue hydration are probably too high to develop uniform equations to assess ICW and BCM.[32]

Mean TBW was reasonably well predicted in both controls and HIV subjects by the three model impedance predictors (Cole–Cole model, an inductor circuit and a modified circuit model).[100] However, the application of the HIV-derived predictors to the control group underestimated TBW, whilst the predictor derived in the control group overestimated TBW in the HIV subjects. ECW was poorly predicted in both subject groups by any of the predictors as indicated by poor correlations (0.29–0.43), biases ranging from 6.1% to 21% and wide limits of agreement. The authors[100] found that algorithms derived in one group of subjects are not necessarily equally accurate when applied to another group of subjects with differing characteristics. The lack of portability of empirically derived algorithms, particularly for the estimation of ECW, implies an inadequacy in the fundamental model underlying estimation of body fluids by MF-BIA and BIS.[100]

Although the relationship between fluid removed during hemodialysis and BIA indices were well correlated in individual subjects, the gradients of the relationships varied considerably between subjects.[126] The overestimation of fluid loss may be affected by shifts in ion concentration, variable changes in impedance as a result of differential loss of fluid from different body segments and postural changes.[126] Scharfetter et al.[116] estimated that, due to electrolyte changes, at the end of dialysis, the error with respect to the volume change was large (up to 15% for ECW and $>$20% for ICW). The authors concluded that a correction of the fluid distribution model for resistivity changes is necessary to obtain more reliable intracellular volume data.

Table 6 BIA studies evaluating TBW, ECW and ICW in subjects with altered hydration

Author	Subject group	*n*	BIA parameter	Reference	Method/equation used	Instrument	Mean bias ± SD or 95%CI[a]	*r*	SEE	Comments/appreciation	Study type; Limitations (L)
Martinoli et al.[81]	Various		Meta-analysis							SF-BIA and BIS significantly overestimated TBW in healthy individuals, whereas there was no overestimation by MF-BIA. MF-BIA seems to be a more accurate method for determining the TBW compartment for healthy and obese adults and for persons with chronic renal failure	Meta-analysis
Healthy subjects											
Gudivaka et al.[82]	Healthy subjects	28	TBW		R_{50}, R_{50p}, X_{50p}, R_{ecf}, R_{icf}, BIS, depending on model used	Xitron		0.96–0.97	2.0–2.4	Cole model is useful to assess body fluid compartments in subjects with altered ratio of ECW-to-ICW. In this short-term within-subjects paradigm, the authors found an accuracy of 0–200 ml and a precision of 500–800 ml when other biological effects that influence impedance independent of volume were eliminated. If the goal is to assess small changes in fluid volume, it is necessary to demonstrate that the results are not influenced by changes in specific conductivity or orthostatic effects	*B*
			ECW					0.84–0.95	1.0–1.5		
			ICW					0.45–0.95	1.5–3.5		
Deurenberg et al.[83]	Healthy subjects	48	TBW	^2H_2O-NaBr	MF-BIA, BIS	Xitron		0.96–0.98		Modelling impedance data has no advantage over impedance values measured at fixed frequencies in healthy individual with normal body water distribution	*B*; *R*
			ECW					0.94–0.95			
De Lorenzo et al.[84]	Healthy subjects	14	TBW	^2H_2O-NaBr	Hanai mixture	Xitron		0.95	1.33	Results support the validity of the Hanai theory and the conclusion that ECW and ICW can be predicted by this model in healthy subjects	*B*
			ICW					0.87	1.69		
			ECW					0.91	0.9		
		73	ICW	TBK	Hanai mixture	Xitron		0.85	2.22		
Olde Rikkert et al.[85]	Elderly	53	ΔTBW ΔECW	^2H_2O-NaBr	MF-BIA	Human-IM			TBW 11%, ECW 10–18%	Detection of dehydration or overhydration based on a single MF-BIA measurement is not possible. MF-BIA correlated well with changes in weight and body fluid compartments in patients going from overhydration to euvolemia, but not from dehydration to euvolemia. MF-BIA cannot detect changes in the distribution or movement of fluid between ICW and ECW space	*B*
Berneis and Keller [86]	Healthy subjects	8	TBW, ECW	Plasma Na, K, H_2O balance	MF-BIA	Data input				Measurement of TBW using BIA under unknown hydration status and unknown osmolality may not be reliable, because BIA is disturbed by altered plasma sodium levels	*A*; L: small sample size; hydration status based on plasma osmolality, not TBW and ECW

Table 6 (*Continued*)

Author	Subject group	*n*	BIA parameter	Reference	Method/ equation used	Instrument	Mean bias±SD or 95%CI*	*r*	SEE	Comments/appreciation	Study type; Limitations (L)
Pregnancy											
Van Loan et al.[87]	Pregnant women	10	TBW	^2H_2O	BIS	Xitron		0.77–0.93	1.6–3.0[b]	No significant differences between BIS and dilution estimates of TBW and ECW. More research is needed to determine population-specific resistivity coefficients	*B*; L: small sample size
			ECW	NaBr				0.41–0.74	1.2–3.4		
Löf and Forsum[88]	Pregnant women	21	TBW	^2H_2O	BIS	Hydra 4200	14 week −1.1±2.3 32 week −3.8±2.9	14 week 0.13. 32 week–0.39		BIS estimated increases in ICW accurately, whereas increases in ECW and TBW tended to be underestimated. BIS may be useful in pregnancy, but that further research is needed	*B*
			ECW	NaBr	BIS		14 week −0.8±1.7 32 week −3.1±1.5	14 week −0.16, 32 week −0.57			
Various diseases											
Simons et al.[89]	Cancer	41	TBW	^2H_2O	SF-BIA	RJL	1.6; 0.2; 3.2			Equation developed in normal weight subjects overestimated TBW in underweight subjects	*B*
Simons et al.[90]	Cancer	33	ΔTBW	^2H_2O	SF-BIA	RJL		0.81		Ht^2/R was significant correlated with ΔTBW. However, precision of prediction of TBW changes was poor	*B*
Cornish et al.[91,92]	Lymph-edema in breast cancer	20			Segmental MF-BIS					Lymphedema was detected by MF-BIA up to 10 month before the condition could be clinically detected	*C*: L: parameters not compared to reference method
Baarends et al.[93]	COPD	77	TBW	^2H_2O	BIS	Xitron		*M*=0.88, *F*=0.85	*M*=2.3, *F*=2.9	TBW by BIS not significantly different from actual TBW. TBW bias and error were comparable to SF-BIA	*B*
		77	ECW	NaBr	BIS	Xitron		*M*=0.75, *F*=0.73	*M*=1.4, *F*=1.2	ECW by BIS was not significantly different from actual ECW, but showed large errors and low correlation compared to studies in healthy subjects. ECW prediction error unable to predict fluid shifts in individual patients	*B*
Steele et al.[94]	Chronic cardiac failure	12	TBW	^2H_2O	SF-BIA	Holtain	2.4; −1.4; 8.9			Although there was a strong correlation between dilution methods and SF-BIA, BIA overestimated TBW	*B*; L: small sample size
Van den Ham et al.[95]	Post kidney transplant	77	TBW	^2H_2O	BIS	Xitron	0.7±2.1 l			BIS is suitable for measurement of TBW	*B*
		77	ECW	NaBr	BIS		3.3±1.8 l			BIS significantly underestimated ECW and is not suitable for measurement of ECW	*B*
Buchholz et al.[96]	Paraplegic patients	31	TBW	^2H_2O	Population-specific	N/A		0.91	2.5	Suggests need for populations-specific BIA equations; equations require further cross-validation. MF-BIA did not improve prediction of TBW or ECW	*B*
			ECW	NaBr	Population-specific			0.81	2.4		

Desport et al.[97]	ALS	20	TBW_{100} TBW_{50}	^{18}O	Vache et al.[119]	Analycor3	0.76±1.85 1.21±1.89			Acceptable estimation of TBW for TBW_{100}; less accurate and concordant at TBW_{50}	*B*
Rutkove et al.[98]	Neuro-muscular disease	45 cont, 25 pt				RJL				Phase angle reductions correlated with disease progression and normalization of phase angle correlated with disease remission. Localized BIA may play a role in the therapeutic evaluation of neuromuscular disease	*C*; L: parameters not compared to reference method
Scalfi et al.[99]	Anorexia nervosa	19	TBW	$^{2}H_2O$	Population-specific	RJL	0.5±1.7			BIA at 100 kHz can be used to predict TBW in anorexia women at the population level, but the individual bias is sometimes high	*B*; L: small sample size
Ward et al.[100]	Controls	27	TBW	$^{2}H_2O$	Various model, see Ref. [100] for details	SFB2		0.86–0.87	3.08–3.40	A Cole model, an inductor circuit model and a modified circuit model predicted TBW well in both controls and HIV subjects. Best predictors were based on estimates of Rtbw derived from polynomial fits and worst predictor was Z-Cole. Application of the HIV-derived predictors to the control group underestimated TBW, and predictor from control group overestimated TBW in the HIV subjects	*B*
	HIV	33	TBW	$^{3}H_2O$				0.90–0.92	2.33–2.50		
Ward et al.[100]	Controls	27	ECW	NaBr	Various model, see Ref. [100] for details	SFB2		0.76–0.79	3.00–3.05	Algorithms derived in one group are not necessarily equally accurate when applied to another subject group with differing characteristics as indicated by poor correlations (0.29–0.43), large biases (6.1–21%) and wide limits of agreement when algorithm is applied to alternate subject group. Lack of portability of empirically derived algorithms, particularly for ECW estimation, suggests that the fundamental model underlying estimation of body fluids by MF-BIA and BIS is inadequate	*B*
	HIV	33	ECW	NaBr				0.54–0.55			
Earthman et al.[101]	HIV	21	TBW	$^{2}H_2O$	$Hannan_{R200}$[120]	Xitron		0.97	1.2	TBW prediction by Kotler gave highest correlation and lowest SEE	*B*; L: small sample size
			TBW		$Hannan_{R500}$[121]			0.95	1.4		
			TBW		$Kotler_{Z50}$[22]			0.97	1.2		
			TBW		BIS			0.90	2.0		
			ECW	NaBr	$Hannan_{R5}$[120]			0.80	1.4	Subtraction of ICW from TBW produced best correlation and SEE for ECW	
			ECW		Kotler TBW_{Z50}—ICW_{Xc50}[22]			0.89	1.1		
			ECW		BIS			0.78	1.5		
			ICW	$^{2}H_2O$-NaBr	Hannan TBW_{200R}—ECW_{5R}[120]			0.87	1.7	ICW prediction for all 4 methods evaluated was similar	
			ICW		Hannan TBW_{500R}—ECW_{5R}[120,121]			0.84	1.9		
			ICW		$Kotler_{Xc50}$ (22)			0.88	1.7		

Table 6 (*Continued*)

Author	Subject group	*n*	BIA parameter	Reference	Method/ equation used	Instrument	Mean bias ± SD or 95%CI*	*r*	SEE	Comments/appreciation	Study type; Limitations (L)
			ICW		BIS			0.81	2.1		
Earthman et al.,[101] prediction of longitudinal change in TBW, ICW and ECW with anabolic steroid treatment	HIV	21	ΔTBW	^2H_2O	Hannan$_{R200}$[120]	Xitron	1.1	0.82	1.5[b]	Δ TBW by BIS and R_{500} was not different from dilution-determined TBW Δ. Further research is necessary to confirm these results	*B*; L: small sample size
			ΔTBW		Hannan$_{R500}$[121]		0.2	0.82	1.4[b]		
			ΔTBW		Kotler$_{Z50}$[22]		0.9	0.81	1.5[b]		
			ΔTBW		BIS		0.7	0.73	1.7[b]		
			ΔECW	NaBr	Hannan$_{R5}$[120]		0.3	0.73	0.8[b]	RSME was larger than the average dilution Δ in ECW. The ECW Δ was too small to draw any conclusions	
			ΔECW		Kotler TBW$_{Z50}$−ICW$_{Xc50}$[22]		0.2	0.79	0.7[b]		
			ΔECW		BIS		0.4	0.75	0.8[b]		
			ΔICW	^2H_2O-NaBr	Hannan TBW$_{200R}$−ECW$_{5R}$[120]		−1.4	0.68	1.5[b]	ICW Δ by BIS was not different from dilution-determined Δ in ICW. ICW Δ was poorly predicted by BIA at frequencies below 200 kHz. ICW Δ predicted by TBW$_{500R}$−ECW$_{5R}$ was closer to, but statistically different from dilution-determined ICW Δ. Systematic error was 12–13% of the average measured Δ in ICW	
			ΔICW		Hannan TBW$_{500R}$−ECW$_{5R}$[120,121]		−0.5	0.67	1.4[b]		
			ΔICW		Kotler$_{Xc50}$[22]		−1.2	0.64	1.5[b]		
			ΔICW		BIS		0.2	0.59	1.6[b]		
Schwenk et al.[102]	HIV	42	ICW	TBK	Kotler[22]	Data Input	1.6; −1.8; 4.9	0.73		BIA is unreliable in this population compared to better established estimation of TBW or ECW	*B*
					Data Input		1.2; −2.2; 4.6	0.73			
					Paton[122]		0.1; −3.4; 3.7	0.72			
					Cornish[123]		4.0; −0.1; 8.1	0.62			
					Xitron		2.9; −1.9; 7.7	0.58			
					Xitron HIV		−1.6; −6.2; 3.0	0.57			
Kotler et al.[22]	HIV	134	TBW	^3H_2O	Kotler[22]	RJL		0.92	7.80%	Disease (HIV) did not affect the prediction of TBW	*B*
Soderberg et al.[103]	Congestive heart failure	12	ΔTBW	Δ weight	BIS	Xitron		0.11		BIS corresponded well to weight changes at the group level, but correlations were poor in individual patients with acute congestive heart failure undergoing diuretic treatment	*C*; L: small sample size; TBW not measured by reference method
Carlson et al.[104]	Laparoscopic and open abdominal surgery	24	ΔZ	Δ weight	SF-BIA	EZ COMP 1500				Impedance did not correlate with changes in net postoperative fluid balance in laparoscopic and open abdominal surgery	*C*; L: parameters not compared to reference method
Tatara and Tsuzaki[105]	Abdominal surgery patients	30	ΔECW	net fluid balance	BIS	Xitron	0.03 ± 0.37	0.89		Segmental BIA[124] can determine fluid accumulation in the trunk during surgery, and monitor perioperative ECW redistribution	*C*; L: parameters not compared to reference

										method
Gonzales et al.[106]	Cardio-pulmonary bypass	18	ΔR	cumulative fluid balance	SF-BIA	RJL		0.81	2.30	Relative day-to-day Δ in whole body resistance may be more appropriate than calculating absolute fluid changes over time	*C*; L: small sample size; parameters not compared to reference method
		18	ΔR	Δ weight	SF-BIA	RJL		0.89	2.07		
Bracco et al.[107]	Cardiac surgery	26			MF-BIA	University Lausanne				Cardiac surgery produced a decrease in segmental trunk impedance, which suggests that fluid accumulation is more predominant in the trunk	*C*; L: parameters not compared to reference method
Perko et al.[108]	Cardiac surgery	16	ΔTotal *Z* Δ Thoraco-abdominal Z	Δ fluid balance	Segmental BIA		0.0±0.1	0.86 0.87		Alteration in electric impedance closely followed changes in fluid balance during postoperative period	*C*; L: small sample size; parameters not compared to reference method
Patel et al.[109]	Coronary artery bypass surgery	8	TBW	^2H_2O	SF-BIA Kushner[35], BIS	RJL, Xitron	SF 0.8±3.3, BIS 5.6±3.3			SF-BIA was more accurate to predict TBW and BIS to predict ECW than BIS in critically ill patients. However the accuracy and bias need to be substantially improved before these methods are useful at the patient's bedside	*B*; small sample size
		8	ECW	NaBr	SF-BIA Van Loan[40], BIS	RJL, Xitron	SF 1.7±2.7, BIS −1.2±2.0				
Hannan et al.[110]	Surgical patients	29	TBW	^3H_2O-NaBr	TBW	Xitron				MF-BIA compares favorably to BIS. Differences between dilution and MF-BIA or BIS are due to errors in the indirect BIA method, and are due to inhomogeneous nature of body compartments and large variations in cross-sectional trunk, arm and leg area. Methods are limited because large changes in the volume of the trunk result in small changes in total body resistance	*B*
					MF-BIA_{200} BIS			0.94 0.90	2.6 3.3		
		29	ECW	NaBr	ECW $MFBIA_5$ ECW BIS	Xitron		0.86 0.86	1.94 1.90		
McCullough et al.[111]	Cirrhosis with and w/o ascites	21	TBW	^2H_2O	Kushner and Schoella[35] Lukaski et al.[38]	RJL				Good correlation for TBW in controls and patients without ascites, but not in patients with ascites. SF-BIA was unable to determine changes of TBW and ECW after paracentesis	*B*; small sample size
		21	ECW	NaBr	Lukaski et al.[38]						
Borghi et al.[112]	Cirrhosis w/o ascites	34	TBW	^2H_2O	Deurenberg et al.[125], Segal et al.[45]	Human-IM		0.86–0.90	1.8–2.5	MF-BIA was able to estimate TBW and ECW, but SEE were higher in patients than controls	*B*
			ECW	NaBr				0.79–0.85	1.6–2.1		
Lehnert et al.[113]	Cirrhosis	21	TBW	^2H_2O	BIS	SFB2	CI±9.2%[a]	0.89		Despite strong correlations in TBW and ECW, large limits of agreement suggest that MF-BIA technique requires further refinement	*B*; small sample size
		21	ECW	NaBr			CI±14.4%[a]	0.73			
Pirlich et al.[114]	Cirrhosis with and w/o ascites	20	ΔTBW ΔECW	volume of paracentesis	SF-BIA	Data input	TBW-1.4 kg, paracentesis -6.2 l			Measured changes of TBW were low compared with the amount of fluid removed. No significant ECW changes were found even in patients who lost up to 13 l of ascites. Whole-body BIA is unable	*C*; small sample size; parameters not compared to reference method

Table 6 (*Continued*)

Author	Subject group	*n*	BIA parameter	Reference	Method/ equation used	Instrument	Mean bias ± SD or 95%CI*	*r*	SEE	Comments/appreciation	Study type; Limitations (L)
Ho et al.[115]	Hemodialysis	16	ΔTBW	^2H_2O	MF-BIA, BIS	Xitron				to detect changes in peritoneum SF and BIS correlated well with TBW by ^2H_2O. BIS was slightly more precise than linear equation (6.2% versus 6.7%, resp)	*B*; small sample size
Scharfetter et al.[116]	Hemodialysis	6	ECW ICW	Ion concentration	Hanai mixture	Xitron	na; −1.0%; 1.9% na; −1.2%; 2.1%			At the end of dialysis, the error percentage with respect to the volume change was up to 15% for the ECW and > 20% for ICW. The authors concluded that a correction of the fluid distribution model for resistivity changes is necessary to obtain more reliable intracellular volume data	*C*; small sample size; parameters not compared to reference method
Zhu et al.[117]	Hemodialysis	10	ECW	Ultrafiltration	Segmental BIS	Xitron				Segmental BIA detected 100% and 101% of changes in ECW in sitting and supine position, compared to 80% and 65% with whole body BIA. Results required changes in electrode placement, estimation of trunk extra-cellular volume using a new algorithm and consideration of changes in dialysate conductivity	*C*; small sample size; parameters not compared to reference method
Jaeger and Ravindra[118]	Hemodialysis									Because the extrapolation of Recw and Ricw, determined by BIS, into volumetric terms is based on resistivity constants derived regression against NaBr or ^2H_2O from nonuremic subjects, the hydric volumes estimated for dialysis patients from these equations must be interpreted with caution until more data is available	*R*

TBW, total body water; ECW, extracellular water; ICW, intracellular water; TBK, total body potassium; ^2H_2O, deuterium oxide; NaBr, sodium bromide; *R*, resistance; *Z*, impedance; Xc, Reactance; SF-BIA, single frequency BIA; MF-BIA, multifrequency BIA; BIS, bioelectrical impedance spectroscopy.

BIA-2000-M, Data Input, Hofheim, Germany; RJL Systems, Inc, Clinton Twp, MI, USA; Xitron Technologies, San Diego, CA, USA; Human-IM Scanner, Dietosystem, Milan, Italy; Hydra-4200,Xitron, Technologies, San Diego, CA, USA; Analycor3, Spengler, France; Valhalla Scientific, San Diego, CA, USA; Holtain, Holtain Ltd, Crymych, UK; SFB2, SEAC, Brisbane, Australia; EZ COMP 1500, Cranleigh, Birmingham, UK.

A: randomized, controlled clinical trial; *B*: controlled clinical trial, non-randomized; *C*: non-controlled prospective clinical trial; *D*: controlled study of case studies with weak methodology; *R*: review article.

[a]95% confidence interval.

[b]RSME=root square mean error, na=not available.

The BIVA showed that all liver cirrhosis patients with clinically detectable edema fell outside the 50% tolerance ellipse for the healthy population and the progressively greater abnormalities were proportional to the stage of liver failure and the degree of fluid imbalance.[68] Thus BIVA is capable of detecting fluid imbalances, but cannot quantify the fluid volume.

Segmental MF-BIA was significantly more sensitive than circumference measurements both in early diagnosis of lymphedema and in monitoring changes in upper limb following surgery for breast cancer.[91,92] Edema was detected by MF-BIA up to 10 month before the condition could be clinically detected.

Conclusions: Based on these studies in Table 6, we draw the following conclusions:

- Visible edema: Hand-to-foot BIA is not valid. BIS and segmental-BIA require further validation.
- Significantly altered hydration states (e.g. large volume IVs, diuretic therapy, edema, ascites, kidney, liver and cardiac disease, status post major surgery, intensive care, pregnancy): Inter-individual differences of lean tissue hydration are probably too high to develop uniform equations to assess body composition, and thus the application of standard SF-BIA is not appropriate to assess ICW or ECW.
- Dialysis (hemo- and peritoneal) and liver diseases with ascites: Currently, BIA and BIS do not appear to be sufficiently accurate to determine dialysis volume and intraperitoneal fluid changes.
- MF-BIA and BIS may be useful for non-invasive monitoring of metabolic changes in subjects with altered hydration state. However, further validation of MF-BIA and BIS is necessary for clinical application of these methods in abnormal hydration states. The potential of MF-BIA and BIS can only be exhausted if the data are interpreted with adequate algorithm that include reliable data fitting and a valid fluid distribution model which considers tissue inhomogeneities. A valid model must guarantee that extracellular volume changes do not corrupt the intracellular volume and vice versa.
- Segmental BIA may prove to be best in determining abnormal hydration in trunk; however, this method has not yet been sufficiently standardized to be used as a bedside technique.
- BIVA method is able to detect altered tissue electric property in ill subjects and this may be more predictive of prognosis than weight loss.

Future development: Further validations of MF-BIA, segmental-BIA and BIS against dilution methods (bromide, deuterium) is necessary to determine their usefulness in under- or overhydration, as well as in abnormal fluid distribution, such as in case of pregnancy, diurectic therapy, edema, ascites, kidney, liver and cardiac disease, status post major surgery, intensive care or dialysis.

Conclusion

BIA is non-invasive, relatively inexpensive, does not expose to ionizing radiation, has very limited between observer variations and can be performed in almost any subject because it is portable. BIA works well in healthy subjects and chronic diseases with a validated BIA equation that is appropriate with regard to age, sex and race. However, clinical use of BIA in subjects at extremes of BMI ranges and in subjects with abnormal hydration cannot be recommended for routine assessment of patients until further validation has proven for BIA algorithm to be accurate in such conditions. MF- and segmental-BIA may have advantages over SF-BIA in these conditions, but further validation is necessary. Longitudinal follow-up is possible in subjects with BMI between 16 and 34 kg/m^2 without abnormal hydration, but must be interpreted with caution. Further validation of BIA is necessary to understand the mechanisms for the changes in acute illness, fat/lean mass ratios, extreme heights, and body shape abnormalities.

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