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Noninvasive Monitoring to Detect Dehydration: Are We There Yet?

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Abstract

The need for hydration monitoring is significant, especially for the very young and elderly populations who are more vulnerable to becoming dehydrated and suffering from the effects that dehydration brings. This need has been among the drivers of considerable effort in the academic and commercial sectors to provide a means for monitoring hydration status, with a special interest in doing so outside the hospital or clinical setting. This review of emerging technologies provides an overview of many technology approaches that, on a theoretical basis, have sensitivity to water and are feasible as a routine measurement. We review the evidence of technical validation and of their use in humans. Finally, we highlight the essential need for these technologies to be rigorously evaluated for their diagnostic potential, as a necessary step to meet the need for hydration monitoring outside of the clinical environment.

Contents

1. INTRODUCTION

It is common knowledge that we need water to stay alive, and the lay literature abounds with stories attesting to the importance of staying well hydrated and recommendations for how to do so. Yet dehydration is not rare, being a frequent result of illness and a precipitating cause of morbidity and mortality (1). With adequate fluid intake, water balance is maintained physiologically through the kidney and cardiovascular systems. Yet, dehydration can and does occur, even in people with functioning kidney and cardiovascular systems; in these cases, dehydration can be corrected through oral fluid intake and thus it is opportune to correct before it progresses to more serious medical problems. The very young (2–5) and the elderly (6, 7) are more prone to and suffer greater consequences from dehydration. Unfortunately, there is currently a lack of measurement technologies to assess hydration status, particularly in a nonclinical setting. The best available tests include serum osmolality (requiring a blood draw and clinical lab) and weight loss (requiring a baseline and subject to confounding factors). A fairly recent review of symptoms, signs, and minimally invasive tests for identifying dehydration in older people concluded that none were consistently nor reliably useful (8, 9).

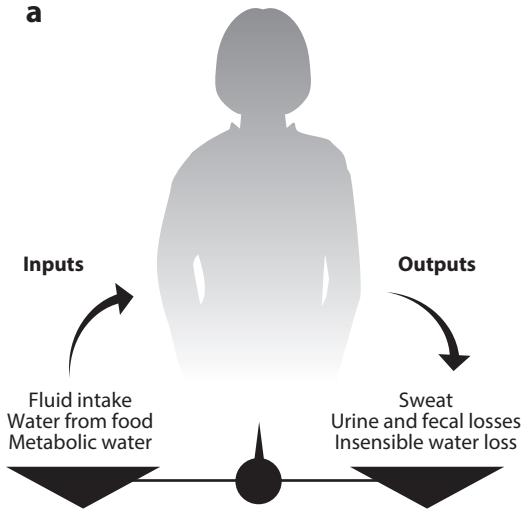
Here we review emerging technologies, with a principal focus on their potential for monitoring outside a clinical environment. We discuss the many technologies that have the theoretical potential to make a measurement related to water or changes in water fraction, although we note

that few technologies have been rigorously evaluated for diagnostic accuracy. Furthermore, none have been shown to work under totally unconstrained conditions. Nevertheless, with these technologies put in context, we have the opportunity to focus efforts on advancing and validating technologies to meet the need for hydration monitoring.

2. OVERVIEW OF DEHYDRATION

2.1. Water Compartments of the Body

Water composes approximately 50–70% of body mass, with the exact proportions depending on variables such as age, sex, and body fat composition (10, 11). Water is distributed among many body compartments (**Figure 1*a***), and under conditions of dehydration, the loss is usually not uniformly distributed across the compartments. Water is also not uniformly distributed among organ systems; for example, fat tissue, bone, and muscles have approximately 15%, 30%, and 70–80% water, respectively (12). For these reasons, when evaluating measures of dehydration, it is important to consider the regions and/or compartments that contribute to those measures.



b	Volume	% of total body water	% of body mass
Total body water	42 L	100%	58%
Extracellular fluids	14 L	33%	19%
Plasma	3.5 L	8%	5%
Interstitial fluids	10.5 L	25%	15%
Intracellular fluids	28 L	67%	39%
Extravascular cells	26.5 L	63%	37%
Blood cells	1.5 L	4%	2%

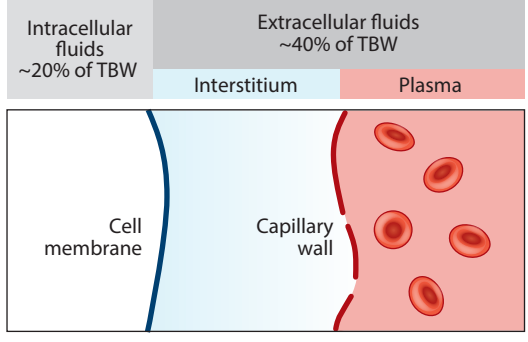


Figure 1

(*a*) The amount of water in the body is modified by the net difference between inputs and outputs (losses). Normally, the inputs are primarily the fluid taken orally (as liquids or in food), and the outputs are primarily excretion by the kidneys and to a lesser extent in the feces. For a person with good renal and cardiovascular function, increases in oral fluid intake are balanced by increases in output, such that overhydration is rare. Decreases in oral fluid intake are also balanced by decreases in output; however, with sustained low intake, dehydration—a decrease in total body water (TBW)—can occur. (*b*) Body water is distributed across the major compartments of the body. To provide a sense of scale, the table and figure show the approximate amount of water in each compartment for a euhydrated 72-kg person. Water can move across compartments, driven by hydrostatic and osmotic forces. Equilibration time (e.g., if one were to inject a small bolus of deuterated water) is approximately 4 h. So, in many contexts (for times longer than 4 h), body water is considered to be in quasi-equilibrium.

2.2. Dehydration Terminology

TBW: total body water

ORT: oral rehydration therapy

Physiologically, the regulation of water balance is tightly coupled to the systems that regulate electrolyte homeostasis and blood pressure (BP). These systems work to maintain an isosmotic serum (normal concentration of electrolytes) to achieve adequate perfusion, during which the degree of their involvement depends on the underlying cause of dehydration (see review in 13). Dehydration refers to total body water (TBW) deficit and can result from any process that leads to a negative water balance (water intake is less than water loss; see **Figure 1**). Note that in people with functioning renal and cardiovascular systems, overhydration is very rare (kidneys will excrete excess fluids). Thus, water deficit is often used synonymously with dehydration.

In cases where the water loss exceeds salt loss (loss is hypotonic), the serum osmolality will rise. Correspondingly, to maintain osmotic equilibrium between the intra- and extracellular compartments, water will exit the cell, such that the distribution of water loss includes both the intra- and extracellular compartments. The combination of water flux out of the cell, kidney retention of water, and thirst aim to bring serum osmolality nearer to isotonic. Several terms have been used to refer to this type of dehydration (14): hypohydration, hyperosmotic hypovolemia, dehydration with minimal salt loss, and intracellular dehydration. By contrast, in cases where the fluid loss is isotonic, serum osmolality remains normal, and the fluid is lost primarily from the extracellular space. This volume loss is "perceived" by baroreceptors, which trigger (among other things) the kidney to retain salt and water to maintain adequate perfusion. This type of dehydration is sometimes referred to as isosmotic hypovolemia, volume depletion, dehydration with salt lost, or extracellular dehydration (14).

Much of the literature does not differentiate between different types of dehydration. In this review, we use the term dehydration to mean loss of body water by any means, and, where possible, we comment on whether particular technologies are more or less suitable for particular kinds of dehydration.

2.3. Treating Dehydration: If You Measure It, Can You Treat It?

The treatment for mild to moderate dehydration is, in principle, simple: increase oral intake of fluids. Fluid intake by mouth is clinically referred to as oral rehydration therapy (ORT), and it is the preferred approach for mild (3–5%) to moderate (6–9%) dehydration because it allows the body's normal regulatory systems to adjust renal excretion of salt and water to restore euhydration (15).

A suitable noninvasive assessment should detect mild to moderate dehydration so that action can be taken before requiring medical attention. With so much attention about the need to stay hydrated, one might guess that dehydration is rare; however, this form of hydration management is open loop—that is, it is done in the absence of objective information. Thirst forms the body's means for self-monitoring for dehydration, but thirst can easily be ignored or overshadowed, and a care provider cannot directly monitor the subject's thirst. Further, many in need of care may not be able to communicate clearly, and the elderly often also suffer from a diminished thirst sensitivity (16). Measurements that can close the loop by providing an indication of changes in hydration status would provide important guiding information to prompt ORT. This is the type of use case we consider in reviewing emerging technologies.

For completeness, we note that, in cases of severe dehydration, the most common approach for rapid rehydration is intravenous (IV) administration. IV fluids are not administered in an at-home setting; they require trained staff to determine the composition and rate of administration for the added fluids, and to monitor the response, as this approach can outpace the ability of the body's regulatory systems to establish proper fluid balance.

2.4. Illustrative Clinical Vignettes

To illustrate the need and the opportunity to detect or monitor for dehydration, we consider three common scenarios in which clinically significant dehydration frequently occurs despite adequately functioning cardiovascular and renal systems. Each of these scenarios could have been mitigated by interventions to increase oral fluid intake.

2.4.1. Clinical vignette 1: dehydration secondary to exposure to a hot environment. Bob is a 48-year-old male factory worker who spent 8 h working in a company warehouse on a hot August day (temperature 102°F/39°C and relative humidity 60%). Unfortunately, upon returning home, he realized that his air-conditioner unit was malfunctioning, so he was only able to turn on a ceiling fan and open his bedroom window, and then he went to sleep. The next morning, he felt weak and lethargic. He decided to go to work, and in the middle of his workday, he started experiencing a pounding headache. He took the rest of the day off and went back home. Finally, after two days of feeling unwell, including nausea and dizziness, he decided to go see his primary care doctor, where he was found to have a resting heart rate of 110 beats per minutes (bpm) (his baseline resting heart rate at prior visits was 60–65 bpm).

Commentary: A clinician would likely immediately suspect severe dehydration due to prolonged excessive heat exposure and high insensible losses, given clinical history and symptoms of headache, lethargy, nausea, and a higher than typical heart rate, along with physical signs of dry skin and dry mouth. Even though the patient had a normal thirst response and access to water, his intakes did not match his outputs. The symptoms of early dehydration are quite nonspecific and can be confused for many other things. Since there isn't a readily available device or tool to measure one's hydration status in a nonclinical setting, most individuals do not know if they are dehydrated, and more importantly, have no clue regarding the degree of dehydration until they suffer an event such as severe dizziness or passing out. So, if there was an accurate, portable, easy-to-use device for at-home monitoring of dehydration, one could proactively assess the amount of water or fluid intake and make sure they are keeping up with high insensible losses, as described in this clinical case vignette.

2.4.2. Clinical vignette 2: dehydration secondary to gastrointestinal illness leading to nausea and vomiting. A mother is concerned about her five-year-old son, as he has had six watery stools in the past 12 h and has been fussy and hasn't had any oral intake (liquids or solids) in the last 24 h. She takes him to the local pediatrician who notices that the child is fussy, but alert and interactive. Vital signs reveal a heart rate of 120 bpm, a BP of 90/60 mm Hg, and a respiratory rate of 36 breaths per minute. The treating clinician tells the mother that it is most likely a viral gastrointestinal (GI) illness, which does not require antibiotics, and that it should get better with time. He advises her to monitor her son's temperature for fever and prescribes ORT. He also asks the mother to take the child to the emergency room if he becomes lethargic or sleepy and has any change in breathing. The next day, the child continues to have watery diarrhea and is now sleepier and less active. The mother tries to give him ORT with some success. She takes the child's temperature and confirms that there is no fever. She continues to give him ORT, as tolerated. The next day, the child is unresponsive to verbal and physical stimulation. She rushes him to the emergency room, where he was found to have a heart rate of 160 bpm, a BP of 70/30 mm Hg, sunken fontanels, dry mucous membranes, and pale conjunctiva. His weight was 4% lower than his baseline weight. He was diagnosed with severe dehydration and was eventually revived with intravenous fluids.

Commentary: The mother was appropriately concerned about loose watery stools and lack of oral intake and did the right thing by going to see a pediatrician. The pediatrician ruled out a

BML: body mass loss

bacterial infection and was appropriately concerned about dehydration, given the history and vital signs, but did not have a way to quantify the severity of dehydration. However, given that the child was alert and interactive, he appropriately recommended ORT and close monitoring. Upon returning home, the mother was unable to quantify oral intake in comparison to fluid loss from watery stools and, thus, was not able to assess the severity of dehydration. She also incorrectly concluded that since this was not a bacterial infection, it was not a serious (life-threatening) issue. Though this child survived, many do not. Dehydration is the leading cause of death for infants and children throughout the world. There were several opportunities in this scenario where dehydration monitoring might have helped avoid escalation to severe dehydration, by unambiguously alerting to progressive dehydration rather than relying on subtle changes in signs and symptoms.

2.4.3. Clinical vignette 3: dehydration secondary to chronically reduced water intake. Agnes, an 82-year-old female with Alzheimer's dementia, has been in a nursing home for the past six months. Over the past few days, she has been more confused than usual and also more fatigued. She barely gets out of bed and has been complaining of palpitations. On one occasion, she almost fell to the ground, and she complained of dizziness. Upon checking her vital signs, she was noted to have a heart rate of 115 bpm and an irregular pulse. Her BP was 90/55 mm Hg. The family was quite concerned and insisted that she be transferred to the hospital for further evaluation. Upon further examination, she was found to have orthostatic hypotension, as well. She was diagnosed with dehydration and admitted to the hospital for intravenous fluids.

Commentary: Agnes's symptoms of fatigue, confusion, palpitations, and dizziness upon standing are all consistent with dehydration. In her case, the dehydration was due to the cumulative water deficit that developed over time because of small differences between intake and output. Though Agnes was clinically evaluated at the insistence of her family, in many cases, it is a fall or a urinary tract infection that is the presenting cause for dehydration in the elderly. There are many reasons why the elderly are particularly susceptible to dehydration, including poor access to water and reduced thirst response. As someone with dementia, Agnes was particularly vulnerable to dehydration. Caregivers provide and encourage liquid intake, but the intake is often limited, such that the fluid deficit grows. In the absence of actionable information, the caregivers in residential (or home) settings must depend on a combination of encouraging fluid intake and monitoring for signs of dehydration. This scenario illustrates a setting in which there is an ongoing and persistent need for an objective hydration measure that could provide actionable feedback to help caregivers know how urgently they need to promote fluid intake.

3. CURRENT ASSESSMENT TECHNIQUES

Clinically, dehydration is assessed on the basis of history, physical signs, and symptoms. The history is usually key, because the signs and symptoms are relatively insensitive to mild and moderate dehydration. Laboratory measures of serum or urine are sometimes used. A fundamental challenge for most of the measures is that the values vary widely across individuals, rendering a static or single-point measure difficult to interpret. In situations for which a baseline is known, changes can be more revealing. Baselines are not usually known when one presents clinically, but they can be determined in the context of a research study or at-home monitoring.

3.1. Gold Standard Measures: Body Mass Changes and Isotope Dilution

There is no accepted gold standard for measuring hydration status (e.g., 17). With appropriately controlled protocols, the closest thing to a gold standard is widely considered to be a body mass loss (BML) of more than 2% [at 2% loss, there is a 90% likelihood of dehydration (18)]. Changes

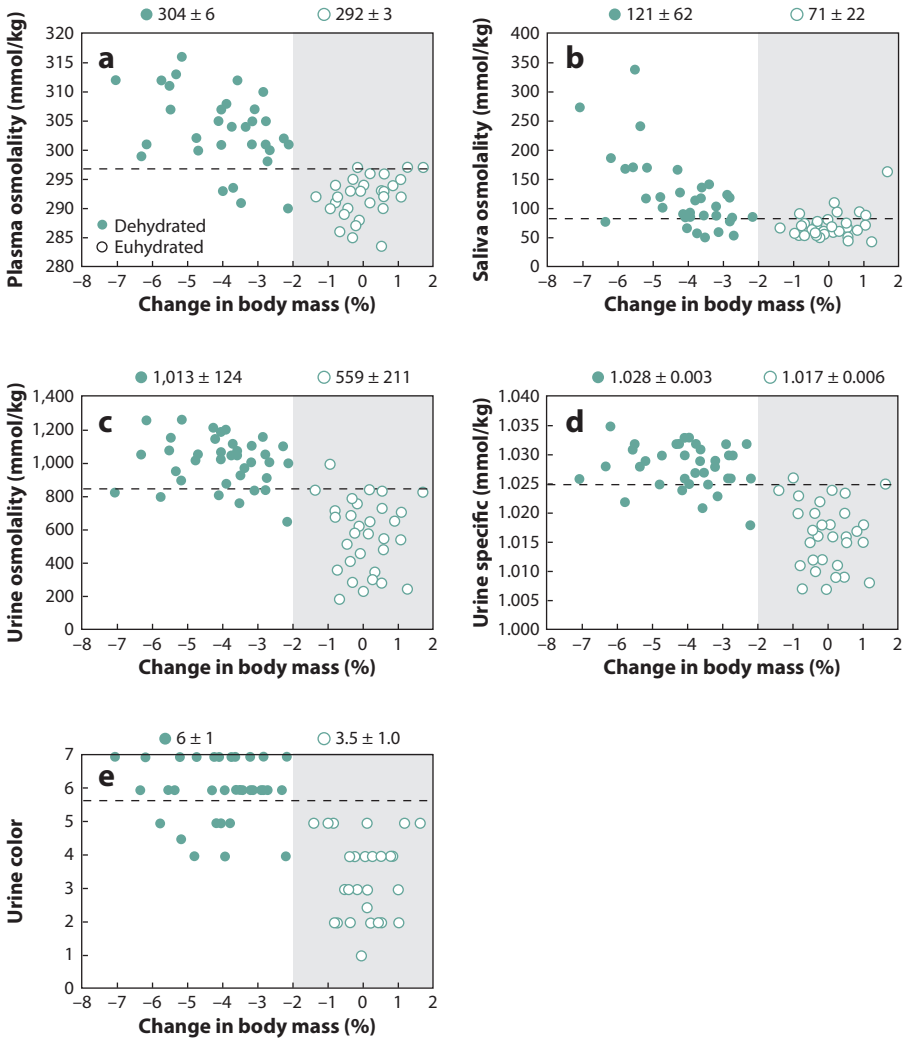


Figure 2

Individual and mean ± SD values of plasma osmolality (*a*), saliva osmolality (*b*), urine osmolality (*c*), urine specific gravity (*d*), and urine color (*e*) plotted as a function of change in percentage body mass when person is euhydrated (*open circles*) and dehydrated (*closed circles*). Data represent 33 (*a*), 35 (*b*), or 36 (*c–e*) pairs of observations from 18 volunteers (5 women, 13 men; 24 ± 4 years old) for whom dehydration was induced through exercise and fluid restriction. The dashed lines represent the diagnostic criterion value (see 18). The shaded and unshaded areas of each plot represent the euhydrated (or nearly euhydrated) and dehydrated states, respectively, as determined from body mass loss. Figure adapted with permission from Reference 18; copyright 2010, Oxford University Press.

in body mass represent changes in TBW, as long as intake is restricted or controlled, and the time over which the change is measured is too short for changes in muscle and fat mass to occur. Body mass changes have been used as a reference measure when evaluating other measurement techniques [e.g., that of Cheuvront et al. (18); see **Figure 2**]. However, this measure provides no indication as to the compartment from which the fluid is lost or gained, and that may be a limitation or complication for evaluating specific technologies during rehydration (17).

Isotope dilution is considered to be the gold standard measure of in vivo TBW (17). Absolute volumes of TBW and differential fluid compartments [intracellular fluids (ICF) and extracellular fluids (ECF)] can be measured accurately and highly reproducibly by measuring the isotope concentration in the blood 3–5 h after bolus isotope administration. However, isotope dilution has no utility as a single-point measure of hydration status, because of the very wide interindividual variation in TBW. Further, the utility for monitoring dehydration via isotope dilution during studies is quite limited because of the time required for equilibration, the need for sophisticated laboratory instrumentation and technical expertise, and the considerable expense.

ICF: intracellular fluids

ECF: extracellular fluids

Posm: plasma osmolality

3.2. Symptomatology

Individual signs and symptoms have been shown to be of low sensitivity for dehydration (9, 19). In an effort to improve diagnostic performance for dehydration, multifactorial assessment scales that combine many signs and symptoms have been developed for clinical use. For example, a prospective study in Rwanda of children presenting with vomiting or diarrhea (mean weight loss of 5%) found that the best-performing multifactorial scale, the World Health Organization scale, had a sensitivity of 68% and a specificity of 21%, and the study concluded that none of the scales were adequate for assessing dehydration status (20). It is reasonable to conclude that when deployed in settings without highly trained clinical personnel, the performance of these symptomatology-related scales would likely be worse.

3.3. Analysis of Blood, Urine, and Body Mass

The most commonly deployed measurements for dehydration are markers in blood and urine, and, as mentioned before, BML. While these markers are widely used, there have been very few studies of their diagnostic accuracy. Two of these include carefully controlled studies of healthy, young individuals to evaluate the diagnostic accuracy of several commonly used dehydration markers after a 1- to 2-day period of euhydration with controlled intake, followed by dehydration induced by exercise and heat exposure (18, 21). The ability of these markers to classify euhydration versus dehydration was estimated from the area under the receiver operating characteristic curve (AUC-ROC). For many markers, the AUC-ROC was >0.7, indicating that the classification is better than by chance, and classification thresholds for the study population show sensitivities and specificities $>80\%$. Caution is advised in generalizing these thresholds, however, because some of these measures have considerable individual and group variability, as is shown by the data of Cheuvront et al. (18) (**Figure 2**; **Table 1**). Indeed, once these variations were accounted for, the authors concluded that for dynamic dehydration assessment, only plasma osmolality (Posm), urine specific gravity, and BML had validity; for static (single-point) assessment, only Posm greater than 301 mmol/kg had validity (demonstrated prospectively) to diagnose dehydration (**Table 1**). As a further cautionary comment, it is unclear whether their results are generalizable to broader populations, since their studies included only a young, healthy population.

Hooper et al. (8) evaluated the diagnostic accuracy of urine markers in older ($\geq$65 years) subjects living in residential care. Of the 283 subjects, 18% were deemed dehydrated on the basis of a Posm $>$ 300 mOsm/kg. They found that urine markers had no diagnostic utility, either alone or in combination. Similarly, in a study of 130 older individuals ($\geq$60 years) presenting to the emergency department or acute care unit, 40% were deemed dehydrated [21% hyperosmotic dehydration with Posm $>$ 295 mOsm/kg and 19% isosmotic dehydration with a blood urea nitrogen to serum creatinine ratio (BUN:Cr) $\geq$20] (19). They concluded that neither the physical signs nor urine markers had diagnostic utility. It is notable that both studies also revealed the high incidence of occult dehydration in the elderly population, reinforcing the need for a noninvasive and convenient means for monitoring.

Table 1 Typical values and diagnostic potential of commonly used biomarkers to detect dehydration[a]

		After 3 days of euhydration					Dehydration induced by exercise and heat				Potential use as a diagnostic for dehydration	
Measure	Units	Mean (SD)	Range	Intraindividual variation	Interindividual variation	Euhydration threshold[b]	Threshold value	AUC	Sensitivity	Specificity	Relative change	Absolute Threshold (SD)
Posm	mmol/kg	292 (3)	284–298	1.3%	1.5%	<290	297	0.95	90	100	9	301 (5)
Sosm	mmol/kg	71 (15)	42–109	9.5%	35.8%		83	0.83	80	83	NS[e]	NS[f]
Uosm	mmol/kg	614 (205)	205–1,091	28.3%	57.9%	<700	831	0.98	91	91	NS[e]	NS[f]
Usg	NA	1.018 (0.006)	1.007–1.031	0.4%	1.0%	<1.020	1.025	0.96	89	91	0.01	NS[f]
Ucol	Scale[c]	2.8 (1.0)	1.0–6.0	30.9%	47.4%	<4	5.5	0.96	81	97	NS[e]	NS[f]
BML	%	0.14 (0.48)	−2.06	1.1%	26.6%	<1%	2.00%	NA[d]	NA	NA	2.5 (~2 kg)	NS[f]

[a]All data if not otherwise noted come from Cheuvront et al. (18).
[b]Data from Cheuvront & Sawka (122).
[c]Data from Armstrong et al. (123).
[d]Dehydration defined as >2% BML.
[e]Measurement not suitable for detecting dehydration from a relative change (dynamic measurement), primarily because the individual variations during euhydration are comparatively large.
[f]Measurement not suitable for detecting dehydration from a single measurement, in part because the interindividual variation is too large to have a reliable threshold.
Abbreviations: AUC, area under the curve; BML, body mass loss; NA, not applicable; NS, not suitable; Posm, plasma osmolality; Sosm, saliva osmolality; Ucol, urine color; Uosm, urine osmolality; Usg, urine specific gravity.

4. CONCEPTUAL FRAMEWORK FOR EVALUATING TECHNOLOGIES FOR HYDRATION ASSESSMENT

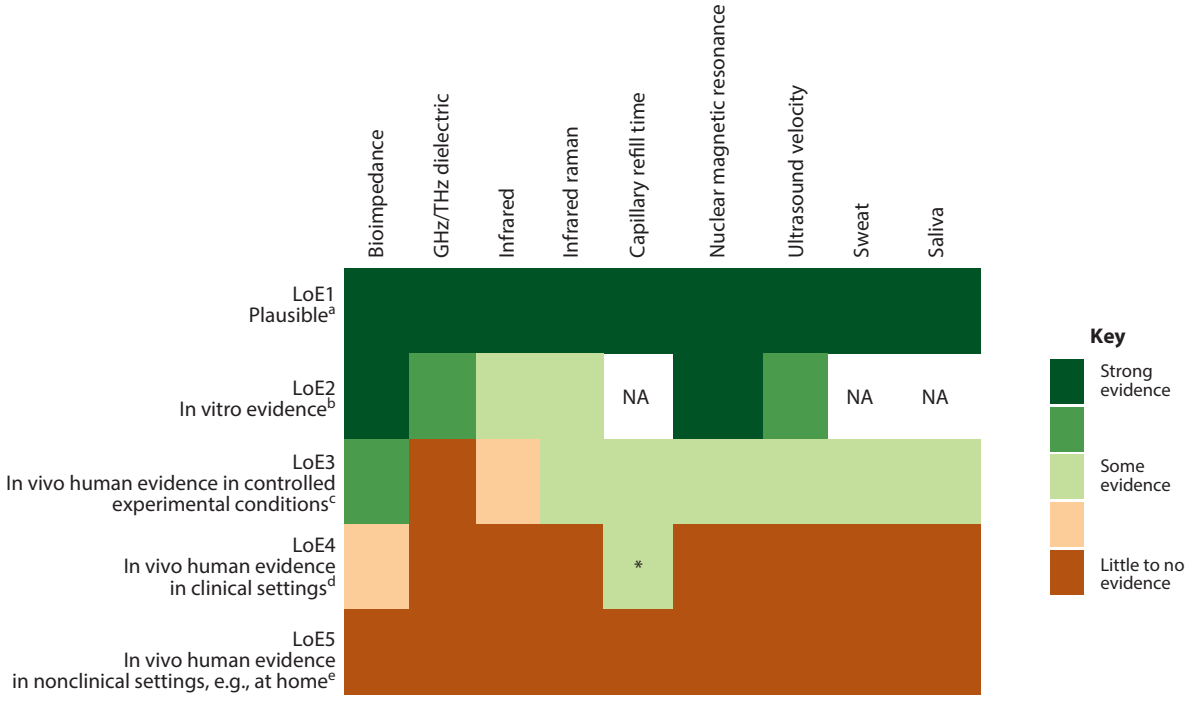
LoE: level of evidence

Given the complexity of hydration-related physiology and the lack of a real gold standard for reference, it is important that we evaluate technologies in the context of their intended uses. As already noted, there are several typical scenarios for which otherwise healthy people can develop clinically significant dehydration and for whom a technology able to detect or monitor their hydration status could provide timely alerts to increase fluid intake, thereby reducing the chance of progressing to a point where the serious sequelae of dehydration ensue. It is these types of scenarios that we focus on in this review.

The most straightforward way to test a new technology is to compare it in head-to-head studies with a well-known and agreed-upon gold standard. That approach is possible when the new technology is intended to substitute in some way for an existing technology—something that does not exist for hydration monitoring. An alternative approach is to build evidence through bench and human studies, ideally reaching the point where the technology can be shown to have sufficient diagnostic accuracy in determining that a state of dehydration has been reached. Given the relatively early developmental stage of hydration-assessment technologies, we use a level-of-evidence (LoE) framework adapted to the particulars of hydration assessment (see footnotes of **Figure 3**). Technologies need to reach LoE4 or LoE5 to become a viable asset to hydration assessment.

In evaluating the published studies related to dehydration monitoring, we note a few considerations and generalizations for those involving human studies:

- Study population: Most human studies have involved young (20- to 30-year-old) individuals; there are relatively few studies of the more vulnerable elderly and pediatric populations.
- Dehydration scenario: Most studies have used heat and/or exercise to induce dehydration. Physiologically, this mechanism of dehydration leads to an increase in Posm and a shift of fluid from the intracellular space to the extracellular space (accordingly it is called intracellular dehydration or hyperosmotic dehydration). The technology may not generalize to other dehydration mechanisms (e.g., diuretics) when the dehydration-induced salt and water shifts will differ.
- Reference measure: The choice and validity of the reference measure is critical, as this measure forms the ground truth in classifying whether the individual is dehydrated. BML is the most reliable measure of water loss in cases where intake is controlled. Isotope dilution is a validated reference measure for TBW and extracellular fluid; however, because it requires a 3- to 4-h equilibration time, it is not practical for dynamic dehydration situations.
- Static or dynamic measurement: Static or single-point measurements aim to provide the hydration status of the individual under study without reference to a baseline. For most measurement approaches, this is not feasible because of large interindividual differences. Dynamic or multipoint measurements reveal a change, generally from a euhydrated baseline. This is the only viable strategy for most technologies, but notably, real-world use will depend on establishing a means for knowing the baseline.
- Native variability: When making repeated measurements for an individual maintaining a euhydrated state, variations in those measurements are to be expected. The change or difference said to indicate dehydration is necessarily larger than this variation (see 13 for a nicely detailed exposition on using these measures of variation to evaluate hydration measurement approaches). Unfortunately, there is very limited information about these variations for the types of devices reviewed here.



[a]There exists a theoretical basis for the approach

[b]There is experimental support for the approach, using model systems or similar

[c]There is experimental evidence that the approach is sensitive in detecting hydration or changes in hydration for the study group when conditions are under experimental control

[d]There is experimental evidence that the approach could serve as a screen for or diagnosis of dehydration in a generalized clinical population or subpopulation (allowing for skilled application of the approach)

[e]There is experimental evidence that the approach could serve as a screen for or diagnosis of dehydration in a generalized nonclinical population or subpopulation (allowing for unskilled application of the approach)

* In a severely dehydrated pediatric population

Figure 3

Comparison of technologies in terms of the LoE to support their use in measuring hydration status. Abbreviations: LoE, level of evidence; NA, not applicable.

5. CURRENT AND EMERGING TECHNOLOGIES

By way of overview, current and emerging technologies employ many different approaches to inferring differences or changes in hydration status (**Table 2**). A few involve direct measurement of a body fluid, such as saliva or sweat. Many involve interrogation of the tissue with electromagnetic energy probes, by measuring a response to an electromagnetic input signal. The tissue volume probed by these technologies ranges from a significant portion of the body to a localized region, depending on geometry, frequency/wavelength, and type of response (attenuation, absorption, scattering, etc.; see **Table 2** and **Figure 4**).

With respect to LoE (**Figure 3**), all approaches, on the basis of physical principles, are sensitive to water and so could conceivably provide a measure of dehydration; therefore, they fulfil LoE1. Only a few have been used clinically [such as bioimpedance and capillary refill time (CRT)], though reliability outside of the context of a given study population has not been fully demonstrated. None have been developed to the point where there is evidence that they could be used at home or in

Table 2 Overview of current and emerging technologies for assessing hydration status

Domain	Technology	Water volume inferred from	Sample volume
Electrical	Bioimpedance spectroscopy	Ionic conduction (impedance for frequency <500 kHz)	Volume encompassed by the path of electrical current flowing between electrodes
	Gigahertz dielectric spectroscopy	Dielectric impedance	Volume between transmit and receive antennas
			Volume near-field coupled by RF probe
	Infrared attenuation	Water Atomic/electronic losses	Optical scattering "banana"
	Raman spectroscopy	Water Dipolar, atomic	Unknown (could be tuned with optics)
Magnetic	Nuclear magnetic resonance relaxation	T1 and T2 relaxation	Total water within section of finger in device
Chemical	Sweat	Na^+, K^+, H^+ NH_4^+, $Ca2^+$, Cl^-	Naturally excreted sweat
			Electrically induced excreted sweat
	Tears and saliva	Osmolality Flow rate	Naturally excreted tears or saliva
	Urine	Osmolality Specific gravity	Untimed or timed void volume
Circulation	Capillary refill	Rate of capillary refill	Approximate peripheral blood flow

a nonclinical setting to either screen for or diagnose dehydration (**Figure 3**). Indeed, the lack of rigorous evaluation of the diagnostic accuracy of these technologies is a major impediment to their utility, whether in the clinic or outside it.

5.1. Bioimpedance (<500 kHz)

Bioimpedance is far and away the most mature and most studied technology in this area. (Note that, in contrast to general engineering usage, in the context of hydration measurement, the term bioimpedance refers to impedance measured in a frequency range of <500 kHz.) For a detailed review of bioimpedance (for hydration and other applications), the reader is referred to several in depth reviews (22–25). Notably bioimpedance approaches have been examined for a wide variety of applications (detection of skin lesions and measurement of blood flow or respiration, body fat, body water, and more). The discussion here is restricted to an analysis of the level of evidence supporting the use of bioimpedance for the purposes of assessing dehydration in humans.

Conceptually, bioimpedance methods rely on the idea that the relationship between voltage and current measured between electrodes will depend on the resistance (impedance) of the material (e.g., tissue), which is, in turn, related to the volume through which the current flows. While conceptually straightforward, interpreting bioimpedance measurements is challenging because of confounds related to tissue/body geometry and structure. Much work has been done to explore the electrical properties of tissues in vitro [see 26–30 and, e.g., the compendium by Geddes & Baker (31) and the review by Foster & Schwan (32)]. As would be expected, these data show that impedance depends on factors including tissue orientation [e.g., for muscle (32) and tissue type/composition/cell density (31, 32)]. Despite the complexity, there is strong in vitro evidence that within a given system (such that structure, orientation, etc., are constant), differences in water content are associated with differences in impedance (e.g., 33).

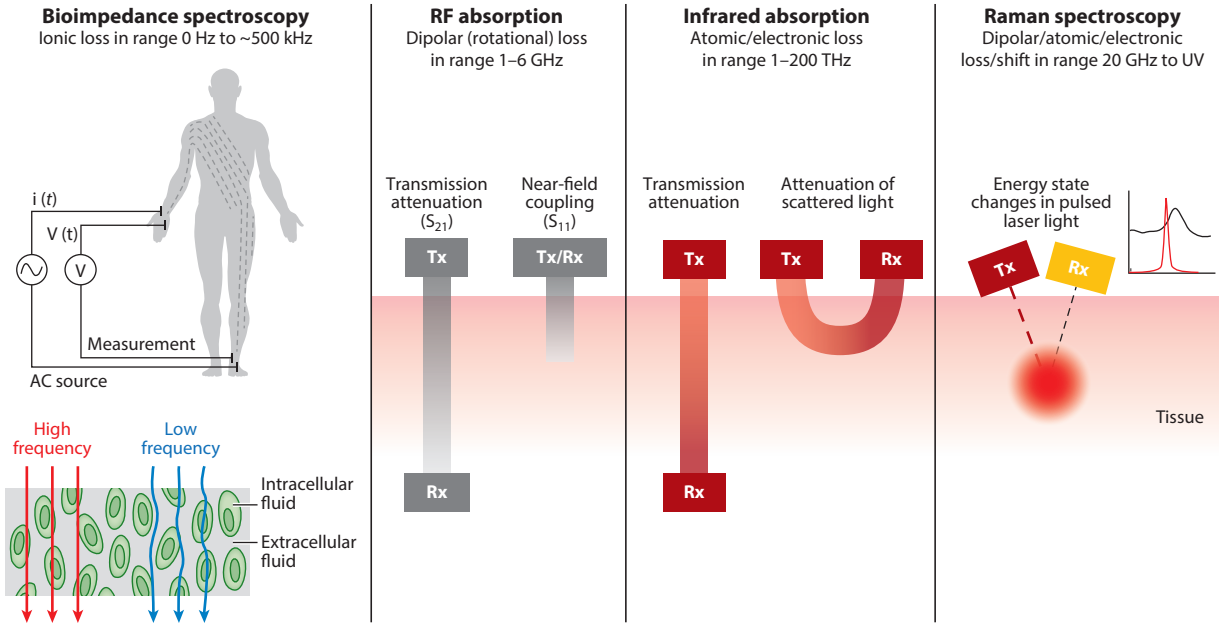


Figure 4

The region and volume of tissue probed by a particular technology depends on geometry, frequency, and type of measurement. Bioimpedance spectroscopy probes the volume subsumed by current flowing between electrodes. Typically, these are on the ankles and contralateral wrist, such that the volume probed includes one upper and lower limb and much of the torso, as shown by the gray dashed lines. At lower frequencies, approximately <100 kHz, the current is excluded by the capacitor-like phospholipid cell membrane, so the region probed is extracellular fluid. Measurements of tissue water content via RF interrogation can, in principle, be conducted in transmission mode measuring the attenuation in tissue between a transmitter (Tx) and receiver (Rx) (a so-called S_{21} measurement) or the near-field coupling of a single probe/antenna and tissue region (a so-called S_{11} measurement). Measurement of infrared absorption can also be achieved through the use of Tx and Rx, with one technique being to place both in close proximity on the same surface, to measure the absorption of backscattered light between the two. By virtue of the Raman shift that happens when infrared light interacts with water, Raman spectroscopy provides a way to measure water content in a tissue region illuminated by a laser light source and a receiver to measure attenuation and shift in the wavelength of the backscattered light.

In short, in vitro studies are consistent with biophysical theory (23, 33) and support the notion that bioimpedance is influenced by tissue hydration, but they also reveal the considerable complexity in establishing a generalizable relationship between impedance measurements and hydration or water content.

Since the 1980s, when bioimpedance devices became commercially available, many studies have reported on the relationship between measures of TBW or fat-free mass (FFM) and impedance (resistance and reactance) measurements (22–25, 34–38). Most commonly, the measurement is made by applying a current between two electrodes placed at the wrist and contralateral ankle and then measuring the induced voltage (magnitude and phase) with two additional electrodes, also placed at the wrist and contralateral ankle. A conducting gel is used to ensure good electrical coupling between the skin and electrode.

While the basic biophysical principle of the measurement is clear and has been validated, when implemented for the human body, the measurement depends not only on water content but also on body geometry and composition (salt, fat, etc.). Indeed, the volume interrogated by the measurement is not the whole body but rather the volume comprising the current flowing between the ankle and wrist electrodes; in turn, that volume depends on body size and shape and, importantly

FFM: fat-free mass

for reproducibility, the position of the limbs. The extreme complexity of that relationship has led to the need for an empiric approach to establishing predictive equations to compute TBW from the measurement.

BIA: bioimpedance analysis

BIS: bioimpedance spectroscopy

A short comment is needed here on terminology: Many published reports involving bioimpedance measures use the term bioimpedance analysis (BIA) to refer to estimates of TBW made from impedance measured at a single frequency and the term bioimpedance spectroscopy (BIS) to refer to estimates made from impedance measured at multiple frequencies.

To summarize the general findings, studies convincingly show a strong correlation between TBW estimated from bioimpedance measures (at 50 kHz or 100 kHz) and TBW measured from isotope dilution (or computed from measures of FFM), with correlation coefficients typically >0.9 and standard error of the estimate typically <3 kg for a broad range of subjects ranging in age from premature babies (39) to children and adolescents (39, 40) to adults (39, 41–43) up to the age of 92 years old (44). Notably, these studies have aimed to standardize the clinical conditions (euhydrated subjects, supine posture, minimal variations in temperature, consistent electrode placement and contact). Virtually all the approaches for deriving the predictive equations to estimate TBW involve finding parameters that provide the best fit with the reference (ground truth) measurement. These predictive equations are often expressed as a function of $\frac{Ht^2}{R}$, where R is the measured resistance and Ht is height (a dependence that is meant to account for differences in body size). Many studies have shown improvements in fits by including Ht (to some power), resistance, reactance, gender, and weight.

Equations to predict TBW from impedance were derived using regression to find the best fit with ground truth (isotope dilution) measures (39, 42–44). While the correlation between BIA or BIS and TBW has been shown to be good, the best predictive relationships are limited to the study population from which the relationship was derived. Indeed, many prediction equations use the same variable but have different coefficients for seemingly similar populations (35), so it is not surprising to see that when the predictive equations are used prospectively (on people not in the original study population), the prediction worsens considerably (e.g., see 45). Thus, it is risky to rely on the absolute accuracy of bioimpedance-derived estimates of TBW. Similarly, it is risky to rely on bioimpedance-derived estimates of TBW as a reference method when evaluating other technologies.

Given the large range of normal TBW across any population, if bioimpedance is to be used to detect a change in water, two (or more) measurements would be required. For the few studies that have directly examined this (45–58), there is evidence that changes in hydration can be detected in controlled settings. For example, steady changes in bioimpedance can be observed during hemodialysis (59), in which the electrodes need only be placed once and the subject remains in one position throughout. On the other hand, researchers have noted that the fluid shifts that occur during and between dialysis can make BIS/BIA measurement challenging to interpret (34, 48, 60). A few studies have demonstrated changes in bioimpedance associated with interventions that decrease TBW. In a study that controlled for subject position and environment during bioimpedance measurements, O'Brien et al. (45) showed that dehydration induced by heat or diuretics in nine young healthy males led to corresponding changes in TBW estimated by BIS. They further concluded that the relationship is more reliable when the dehydration happens in a way that increases serum osmolality (e.g., heat) than when there are minimal changes in serum osmolality (e.g., diuretic), though the soundness of this conclusion cannot be assessed without more information (additional protocol details and raw data) and additional subjects.

Though studies have shown an association between changes in TBW and changes in bioimpedance, there are, to our knowledge, no systematic studies evaluating the diagnostic potential of bioimpedance for interventions relevant to the scenarios of Section 3 (e.g., heat or

exercise-induced dehydration). An analysis of individual subject data reported in a study of exercise-induced changes in TBW in 10 young individuals (55) makes it clear that one would have very poor ability to predict the change in TBW from BIS alone on an individual subject, though when all subjects are looked at in the aggregate, the change in body mass trended with change in BIS. In a sense, these challenges were anticipated in the early days of bioimpedance when researchers concluded that hydration state itself is a confounding variable and so hydration state should be assessed before interpreting BIS measurements (46, 47).

Considerable effort has been devoted to exploring possible confounding factors, which, if controlled for, might increase the potential utility and reliability of bioimpedance measurements. Notably, possible confounding factors include (*a*) body posture changes associated with varying electrical path [5.0% and 6.6% TBW error (36, 61)], (*b*) electrode position associated with varying electrical path [1% TBW error/mm (62, 63)], (*c*) electrode contact area associated with skin interface conductivity changes [2% TBW error for 1–3x change in contact area (64)], (*d*) sweat-related salts between the electrode and skin associated with skin interface conductivity changes [1.3% TBW change after alcohol wipe (62)], and (*e*) skin temperature, and its influence on skin blood flow [2% TBW change/°C (65, 66)]. Some of these issues might be overcome by putting electrodes closer together [as is done to measure skin hydration for the cosmetics industry (67)]. However, with closely spaced electrodes, the measurement is dominated by the contact resistance (between the electrode and skin) and the properties of the epidermal layer. Even if those aspects could be controlled for, the change in conductivity due to dehydration would be miniscule for such a short measurement path. Some issues might be overcome by having the electrodes remain in place and by monitoring the environmental and positional factors. Doing so would require a considerable increase in complexity and an evaluation as to whether algorithms can correct for differences in position and environment or can work by using only selected environments/positions for monitoring.

Our conclusion is that, for real-world settings, bioimpedance spectroscopy suffers from many confounding factors that, unless overcome, would challenge efforts to track small to moderate changes in hydration status.

5.2. Gigahertz- and Terahertz-Range Dielectric Spectroscopy

As we move to a higher electromagnetic frequency range (gigahertz and terahertz), the mechanism of interaction of electric fields with water-rich materials transitions from being dominated by conductivity to being dominated by the relative permittivity. Put another way, in contrast to lower frequencies, where the impedance measurement is biased toward a measure of the amount of current that is conducted by the material, at gigahertz and terahertz frequencies, impedance is biased toward a measure of the amount of energy from an external electrical field stored in the material. At all frequencies, the measurement is dependent on the water and, in particular, the volume of water that "sees" the electric field. At high gigahertz and terahertz frequencies, that sensing volume is localized to near the electrode (and depends on frequency and electrode geometry) (68–70). Because of this limited sensing volume, it would not be possible to probe TBW of a human directly due to its size. However, to the extent a localized measurement is reflective of the hydration state, such a measurement could hold promise.

The sensitivity to water at frequencies >1 GHz is well recognized and is supported by theoretical analysis [e.g., Taylor et al. (71), which includes an example of sensitivity to the percentage of water for a mixture of water and lossless biological material]. Experimental measurement of dielectric properties of biological materials is generally done using a coaxial probe and a vector network analyzer; the relationship between the measurement and electrical properties depends

on the geometry of the probe as well as the material under test, but for measurements made with the same probe, variations in the electrical properties of the material will be revealed with the measurement (see tutorials in 72 and 73). Importantly, the volume of material that is probed or "seen" with these probes is restricted to a region near the probe and is strongly dependent on the size of the probe as well as the effective permittivity. For a given probe, the depth of the sensing volume decreases somewhat with increasing frequency, with that depth for typical setups being on the order of millimeters for gigahertz measurements to microns for terahertz measurements (68–70). Importantly, for tissues that are heterogenous within the sensing volume, the material nearest the probe will be more heavily weighted than that further away, and, in turn, the sensing depth itself is influenced by the electrical properties of the materials [e.g., see Porter et al. (68)].

Much of the work in this frequency regime has been motivated by the need to evaluate the safety of exposure to high-frequency fields. With regard to our focus here on measures of tissue hydration, we know of no reports providing a quantitative relationship between hydration of biological tissues to measures of impedance at frequencies >1 GHz. On the other hand, studies done to characterize tissue electrical properties at these frequencies provide evidence of sensitivity to water content. For example, electrical properties of tissues at these frequencies show tissue-dependent properties that are explained as resulting from differences in their water content [e.g., see reviews in 71, 74–76]. Similarly, age-related changes in electrical properties have been attributed to age-related decreases in tissue hydration (77). Additionally, several studies have shown changes in electrical properties in response to a reduction in water content by dehydrating excised tissue and compressing tissue engineered constructs (78–80). Furthermore, these approaches have been used in imaging modes to identify regions of differing water content for potential applications in skin and breast cancer (81, 82) and skin burns (71).

Our conclusion is that there is evidence to support the dependence of dielectric properties on tissue hydration in living tissues. Its use as a measure of hydration status in humans is, as of this writing, unknown.

5.3. Infrared Spectroscopy (300 GHz to 400 THz; Wavelength 1 mm to 750 nm)

Like other higher frequencies in the electromagnetic spectrum, the basis for the use of infrared spectroscopy as a measure of tissue water is based on selecting frequencies for which the influence of water, relative to other tissue components, is the main determinant of the interaction between the tissue and electromagnetic energy. In the infrared regime, this interaction includes scattering and absorption, both of which are highly wavelength dependent (83). While wavelengths in the 400- to 600-nm range have been widely used to measure oxy- and deoxyhemoglobin, longer wavelengths (>900 nm; $f <$ 300 THz) have been used to provide information about tissue water and fat content. At these longer wavelengths, absorbers (chromophores) include water, fat, and collagen (84, 85). A Monte Carlo simulation of photons interacting with a model of skin (melanin-containing epidermis and a uniform non-melanin-containing dermis) revealed that the wavelength-dependent penetration depth can reach more than 5 mm for wavelengths higher than 700 nm (83). In vitro studies of other tissues show that penetration depths depend on frequency and tissue type, but penetration depths of >4 mm for wavelengths in the 1,600- to 1,900-nm range have been achieved (86). In terms of a nonhomogeneous tissue-like skin, Monte Carlo simulations illustrate that intensity drops dramatically (>50%) within the melanin-containing epidermis (83). This effect would be an important consideration in interpreting the overall absorption at these wavelengths.

A few studies report on the use of near-infrared imaging to sense changes in tissue water. Cuccia et al. (87) described a modulated imaging system that provided broadband illumination,

and captured narrowband reflection, from which they determined optical properties (absorption and scattering) on the basis of diffusion and Monte Carlo models. They showed that absorption at 800 nm significantly increased following venous occlusion of the forearm. At 800 nm, absorption by hemoglobin is significant, and it isn't clear how much of the change was due to hemoglobin per se, versus the increased water fraction, but it does suggest that a similar measurement at longer wavelengths, where water would dominate absorption, might have promise. Along those lines, Visser et al. (88) constructed a sensor in which tissue was illuminated with light-emitting diodes (1,300 and 1,480 nm) placed on the skin surface and reflectance was measured with a coplanar photodiode. The composite data reported from nine adults with exercise-induced dehydration provided a general, but noisy, trend in which the reflected intensity from the more dehydrated state was less than that from the euhydrated state. They also showed a decrease in reflected intensity over time when the epidermis was exposed to a wet towel. Though it is difficult to be certain from the report, it appears that the influence of wetting the skin (which presumably affects only the epidermis) was similar to the influence of exercise, raising the question of whether the measurements after exercise could have been confounded by changes in epidermal hydration. The data reported from each of four infants who were given ORT following GI illness–induced dehydration showed that the reflected intensity from the more dehydrated state was much greater than that seen after ORT. Collectively, these results are intriguing but not clarifying. Much work would be required to bring this technology from one that is theoretically viable to one that can actually be used in practice.

5.4. Infrared Raman Spectroscopy

Raman spectroscopy methods have been developed to provide a noninvasive way to assess chemical analytes in tissues and other turbid media (89). In the infrared regime, not only is water a significant absorber but the scattered light exhibits a significant Raman shift. In principle, this offers an alternative way to probe the relative amount of tissue water, and there are a few reports along these lines. For example, Raman spectroscopy of cartilage exhibits multiple peaks resulting from interactions with water (bound and free), collagen, and proteoglycan (90). When the cartilage tissue was air or oven dried, leading to a >70% decrease in wet weight, the Raman intensity decreased roughly linearly with the percentage decrease in cartilage wet weight. It is unclear whether that relationship is maintained for less extreme (and more physiological) changes in water content.

Caspers et al. (91) used the ratio of intensity of Raman bands for water (~3,400 cm^{-1}) and protein (~2,950 cm^{-1}) "calibrated" with ex vivo stratum corneum samples for which water content was measured to estimate water content in vivo. To do the in vivo measurements, they used confocal Raman spectroscopy, so that they could estimate water fraction as a function of depth from the skin surface. Looking at locations on the volar aspect of the forearm and the thenar eminence, they found that water fraction progressively increased from ~30% in the stratum corneal layer to >60% in the dermis. They further reported that, while measurements made at the same location were reproducible, their measurements at nearby locations (of the forearm and thenar eminence) differed significantly from one another. Thus, if this approach is to be used to track hydration, care would be required to take the measurement from precisely the same location. In an intriguing study of younger and older men, measurements of dermal water content using this confocal Raman spectroscopy method were consistent with previous reports that water fraction in older people (60–68 years old) is higher than in younger people (20–24 years old); within each age group, the water fractions differed by ~±3% (92). Furthermore, they reported that dermal water content was slightly greater in the afternoon than in the morning, though this difference seemed to be mainly at depths near the interface between the dermis and epidermis, and no information was provided to determine if this diurnal variation was seen in some or all of the subjects.

Taken together, these studies show that there are data supporting the general idea that Raman spectroscopy is sensitive to differences in water. Further studies would be required to determine whether it holds promise in the context of assessing or monitoring for changes in one's hydration status. And, if such studies are promising, much work would be required to develop the technology so that it would be suitable for home use.

5.5. Capillary Refill Time

The perfusion and dynamics of blood flow in peripheral capillaries presents an easy-to-access indicator for some aspects of circulatory status. Proposed initially as a means to assess shock on the battlefield, CRT has been shown to be related to fluid status (93). Clinically, CRT is measured by pressing on the finger (or other capillary bed) to exude blood from the capillaries, followed by release and measurement of the time it takes for the compressed skin to return from blanched to a normal color, as determined by visual inspection (for illustration, see, e.g., the videos in 94). There is evidence that CRT can be a reliable indicator of severe dehydration in children but little to no evidence of its reliability in adults or in cases of mild to moderate dehydration, likely due to the large number of factors that influence CRT (see 95 and 96 and references therein). In a population of severely (>5%) dehydrated children, Shavit et al. (97) showed that accuracy was improved by analyzing videos of the CRT test, in comparison with conventional manually timed CRT. Numerous patents have been published that seek to automate the CRT measurement. In some cases, the application and release of pressure to remove capillary blood is also automated. So far as we are aware, no commercially available product that provides an automated CRT test exists, and there are no reported studies of the utility of such a product. Prior studies with manual CRT suggest that automating the readout and pressure may not be adequate to overcome the complex factors that determine CRT, except, perhaps, for a select population or circumstance.

5.6. Nuclear Magnetic Resonance

The relationship between tissue composition (including but not limited to water content) and ^{1}H–nuclear magnetic resonance (NMR) or magnetic resonance imaging (MRI) signals is complex and well beyond the scope of this review. Simplistically, magnetic resonance (MR) measurements involve measuring the relaxation of proton (^{1}H) magnetization after stimulation with a magnetic field. T1 relaxation is the return of the magnetization to the initial state; T2 relaxation is the dephasing of magnetization after stimulation. In a simple system, the relaxation is an exponential decay where the initial amplitude is related to the number of protons and the time constant is related to the environment where the protons reside. In multicomponent systems (e.g., one or more tissue types), the relaxation is often multiexponential.

Thus, there is a foundational basis for considering whether MR signals could be used as a noninvasive approach to monitor hydration status. One group has worked to explore and develop this approach while taking into account both the practical challenge of creating a portable (or movable) sensor suitable for use outside of the clinic and the feasibility challenge of determining where to measure and whether the measure is sufficiently sensitive (98). In their early work, they used a benchtop NMR system to measure T2 in mice for differing levels of dehydration. Whole-body T2 relaxation time tended to decrease with dehydration (up to 23% BML) in fluid-restricted mice (~1 ms/% BML, estimated from plotted data). In a separate study (99), the authors took advantage of the capability of the benchtop NMR system to distinguish tissue types (lean, fat, free fluid, and unknown) to look at tissue-specific effects of heat-induced dehydration on T2 (up to 13%). For lean mass (muscle, primarily, and the tissue type expected to change with dehydration), they found that T2 amplitude was lower for states of greater dehydration (~−1% difference from baseline amplitude per 1% BML, estimated from plotted data).

More recently, the same group evaluated MR relaxometry in humans, focusing on dialysis-induced changes in fluid status (100). From T2 images (using a standard MRI system), they computed T2 for muscles in the lower leg. T2 is biexponential, with the longer and shorter time constants thought to reflect ECF and ICF, respectively. They found that the relative proportion of extracellular T2 (long T2) was significantly lower after dialysis. In the same subjects, they also used a custom-built single-sided NMR sensor to make T2 measurements before and after dialysis. This nonimaging sensor senses the local volume, including subcutaneous tissue and muscle. The relative extracellular T2 also was lower after dialysis, but the changes were not as significant as the measurements made from segmenting MRI images and were only interpretable as changes in extracellular volume before and after dialysis rather than absolute values; this result was suggested to be due to the unknown contribution of the subcutaneous tissue in the nonimaging data. Overall, these studies support the notion that MR measures are influenced by hydration; it remains unclear whether a surface NMR sensor can be designed to have sufficient sensitivity to reliably monitor hydration changes under different circumstances or as a single-timepoint measure.

5.7. Ultrasound Velocity

The conceptual basis for ultrasound measures of hydration is that the speed of sound in a bulk material is determined by its molecular composition and short-range interactions between molecules; thus, ultrasound velocity (UV) would be expected to track hydration changes in a setting where the dominant molecular change is that of water content. In vitro evidence of tissues and tissue phantoms support this premise. For example, UV correlates with tissue water content for liver and muscle, independent of orientation, and progressive changes in UV with progressive dehydration could be reliably measured in muscle samples (see 101 and references therein). Importantly, the sensitivity (~3 m/s per 1% change in water) and reproducibility (equivalent to ~0.2% water) suggest that this method shows promise. Several studies of dehydration (exercise-induced) and rehydration in athletes have found, on average, that UV changes (measured at the calf) correspond to changes in serum and urine markers (102, 103); however, there was considerable variation across individuals. Furthermore, UV measured in transmission mode is influenced by tissue fat, such that the change in UV per change in water will differ across individuals (103). Further development of this approach may require a means for ensuring that only muscle is sampled in the measurement and a means for longitudinal monitoring.

5.8. Sweat Composition Analysis

Sweat is, essentially, an exudate of tissue fluid, comprising water and electrolytes. Conceptually, the hypothesis behind wearable sweat analysis sensors is that sweat electrolyte analysis will reveal dehydration-induced increases in tissue osmolality (electrolyte concentration) (104–106).

Investigations of the relationship between sweat electrolyte composition and hydration status have yielded different conclusions. In exercised-induced dehydration studies, Morgan et al. (107) observed that sweat [Na^+] and chloride [Cl^-] increased with dehydration, while other authors observed a decrease (108, 109) or no change (110). Among the reasons for this discrepancy are that sweat electrolyte composition varies among subjects and that the final sweat composition depends on a variety of host and external factors not all related to dehydration (see analysis and table 1 in 111).

Despite the fact that the correlation of sweat electrolyte composition and hydration status is not yet completely understood, the easy accessibility of sweat has caught the interest of developers for the wearable devices market. The analysis of sweat biomarkers has primarily been achieved by using electrochemical sensing (112–115). For dehydration measurements, a fabric-based

conductometric sensor is typically directly worn on the body (104, 116). For example, smart bands that incorporate electrochemical sensors have been developed and have been tested for sweat analysis both indoors on subjects during constant-load exercise on a cycle ergometer with real-time physiological monitoring and outdoors on a group of subjects engaged in prolonged running (104). A substantial increase in sweat [Na^+] and a smaller increase in sweat [K^+] were observed in dehydration trials (without water intake, ~2.5% of BML), and it was concluded that sweat [Na^+] can potentially serve as an important biomarker for monitoring dehydration (104).

Although there are now products on the market that claim to enable hydration monitoring via sweat analysis, to our knowledge none have had rigorous tests published (accordingly, they have disclaimers noting that they are not medical devices but rather fitness trackers). Perhaps their existence will make it more straightforward, efficient, and cost effective to conduct a study to evaluate their performance and diagnostic accuracy. The utility of such sensors also may be limited to use models where the level of sweating is sufficient to garner a sample, which may not include, for example, the latter two of our three dehydration vignettes.

5.9. Saliva Osmolality

The flow and composition of saliva have long been known to be affected by exercise, with numerous studies showing that exercise-induced changes in body mass are associated with decreased flow and increased saliva osmolality (117, 118). The precise physiological mechanisms for this are not fully understood but seem to be related to Posm and to sympathetic nervous system activity (119), both of which are influenced by hydration status. Here we focus on saliva osmolality, as it shows the most promise among the saliva markers. While there are numerous studies documenting a correspondence between changes in body mass (or other markers of dehydration) and changes in saliva osmolality (Sosm) on a study population basis, the few who have designed studies to determine diagnostic accuracy have reported sensitivities of 70–80% and specificities of 70–80% (18, 19). Some diagnostic accuracy may be lost by the sample collection process, leading to an intrasubject variation of ~10% (14, 18). Furthermore, in one of the few studies that examined and reported results on an individual basis, they noted substantial intersubject differences in euhydrated baseline Sosm (precluding the use of a single measurement to assess hydration status) and substantial differences in the change in Sosm per percentage BML (possibly precluding its use as a means of diagnostic monitoring) (117).

6. CONCLUSION AND CALL TO ACTION

Considerable effort in the academic and commercial sectors has been made over the past few decades to provide a means for monitoring a person's hydration status, with a special interest in doing so outside the hospital or clinical setting. Technical validation of these approaches is challenging because of the lack of a robust gold standard. Changes in body mass are the best comparator, but care is required in the study design to ensure that changes in body mass are largely the result of changes in body water and that changes in body water occur in the region being analyzed. To the extent that there are studies to validate the technology, they often report on a population, documenting correlations between the measurement approach and a reference. While that is an important first step, for these approaches to be useful in guiding actions by an individual, it is essential that their diagnostic accuracy be evaluated. While there have been careful studies of the diagnostic accuracy of clinic measures (see Section 3), there are exceedingly few reports evaluating the diagnostic accuracy of technologies that could potentially be used outside of the clinical environment.

The need for hydration monitoring is significant, especially for the very young and elderly populations who are more vulnerable. For individuals with functional renal and cardiovascular systems, it is straightforward to take corrective action—ingesting fluids—should the monitoring warn of dehydration. Without such a warning, people are often unaware until more serious sequelae ensue, in which case dehydration is considered a secondary diagnosis. Consider, for example, studies that have shown that, on the basis of serum markers, the elderly living in long-term care facilities were twice as likely to be dehydrated (22%) as the acutely ill hospitalized elderly (11%). Indeed, over the decade 1990–2000, the rate of dehydration-related hospitalizations in the United States increased by 40.4% (120, 121).

It is exciting that there is great commercial interest in this space and that there are many approaches that, on a theoretical basis, should be sensitive to changes in water. As with any measurement approach, there are myriad potential confounds that need to be explored as part of the technical validation. Perhaps most importantly, as biomedical engineers and consumers, we need to ensure that the device development strategy includes an assessment of diagnostic accuracy. Without that assessment, we will not be able to meet the need for hydration monitoring.

SUMMARY POINTS

1. The need for hydration monitoring is significant, especially for the very young and elderly populations who are more vulnerable to dehydration.
2. Realization of hydration monitoring solutions is lacking, particularly in a nonclinical setting.
3. Many measurement technologies for the quantification of hydration status have theoretical potential and are feasible as a routine measurement.
4. Several proposed technologies have the theoretical potential to be sensitive and specific to water; however, few have been validated for diagnostic accuracy.
5. In terms of a clinically meaningful measurement, most technologies have a greater likelihood of detecting a change in hydration rather than providing a single-point measure of hydration status; thus, a means of establishing a baseline is a necessary but yet-unaddressed requirement moving forward.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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