A Review of Portable High-Performance Liquid Chromatography: The Future of the Field?

Supplementary Information

Faraz Rahimi,[1,2] Stelios Chatzimichail,[1] Aliyah Saifuddin, [1,2] Andrew J Surman,[2] Simon D Taylor-Robinson[1] and Ali Salehi-Reyhani[1]*

1 Dept. of Surgery and Cancer, Imperial College London, London, UK
2 Dept. of Chemistry, King's College London, London, UK
*ali.salehi-reyhani@imperial.ac.uk

Contents

1. BETTER Criteria

The BETTER (portaBle fiEld Testing sTandard framEwoRk) criteria 2020.

System Cost:
As discussed in the text, it is important for miniaturized systems to not only maintain or exceed the typical performance of their laboratory-based counterparts but to do so in an affordable and therefore accessible manner. Within the BETTER criteria, the Grade 1 system cost is comparable to a laboratory-based Agilent 1260 Infinity HPLC (Agilent, Santa Clara, CA, USA). Grade 2 and 3 reflect the likely costs of the prototypes presented to date. Grade 4 and 5 are to be set as a benchmark for future prototypes. For this aspect of the framework to be successful, future prototypes should engage in a level of disclosure to allow non-biased assessment of each system. It is important to note that system cost, if not provided, is estimated using one off costs of the major components required in the system. One-off costs at list price, in contrast to volume pricing, better reflects the investment necessary for a research group to replicate the system or device.

Cost per test:
In the current climate, HPLC tests in centralised laboratories are on the order of \$10s to \$100s US. While the cost per test is subjective and heavily dependent on the type of analysis being undertaken, the BETTER criteria aims to encourage innovative means of analysis which compete with centralised laboratories. For example, as mentioned in the text, green solvent replacements can reduce running costs potentially 10-fold with only minor sacrifices in performance.

Weight:
Once again, the Grade 1 weight is in line with a commercial Agilent 1260 Infinity HPLC. The goal of this criterion is to encourage the field to account for externalities which will affect the end-user's ability to perform HPLC anywhere including solvent/waste reservoirs, computer/controller, power source, and consumables. The weight of these externalities significantly affects the overall weight of the prototype and must be considered in order to allow fair and impartial comparisons.

Portability:
Portability describes the size and form factor of the prototype. It is important to identify this criterion as it allows application-specific systems to arise with features to suit various utilisations. For instance, a particular system may fit into a backpack and may be suitable for use in a remote location such as the Australian Outback. Whereas, another system may be attached to a scrambler motorbike to be used as a portable laboratory. Prototypes reported within the past decade fall into the Grade 3 and 4 categories.

Operation time:
The majority of prototypes presented to date quote an operation time away from mains power between a full working day (Grade 1) up to 24 hours (Grade 2). These can be seen as standard and realistic estimates given that frequent recharging is inconvenient would reduce throughput. System operating times of up to one week, one month, and beyond one month are set as the benchmarks for Grades 3, 4, and 5, respectively. Future prototypes should include operation time using battery power as a standard test alongside analytical performance.

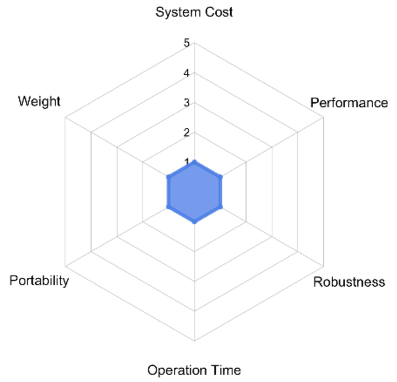
Robustness Testing:
Thus far, with the exception of Chatzimichail et al., robustness testing has been overlooked by the field. Given that the end-goal of portable HPLC is to perform HPLC anywhere, it is surprising to find that durability and robustness testing of prototypes while in operation is not reported. The field should aim to at minimum adhere to the Grade 4 criterion in which the system is 'resistant to shock impacts during operation'. Without meeting this criterion, portable HPLC would become a very expensive feat.

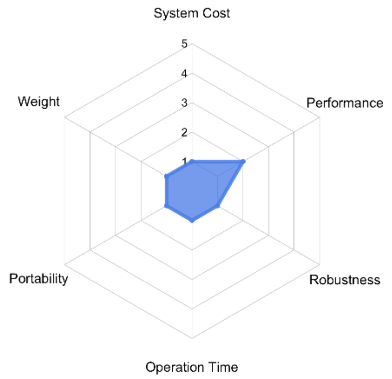
Performance:
The chromatographic performance of the prototypes is classified according to the elution type and operating pressures. Grade 1 and 2 describe systems with attainable pressures of < 50 bar and ≤ 200 bar, respectively, while Grade 3 and 4 are dedicated to systems capable of up to 600 and 1300 bar, respectively. Grade 5 refers to systems with operating pressures above 1300 bar. We acknowledge that this grading may alter with advances in miniaturised pumping technology; however, at this time, we believe that the framework accurately describes the performance of current prototypes.

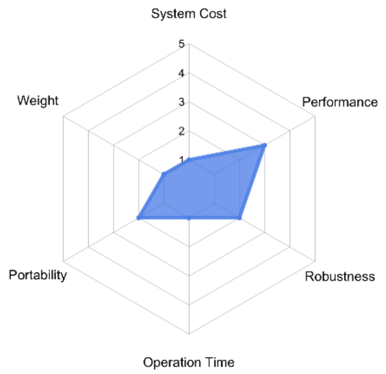
Waste Production:
The volume and handling of HPLC waste are important factors which must be considered for portable prototypes. Ensuring responsible disposal of large volumes of hazardous waste can become expensive, time-consuming, and inconvenient. Grade 1 is in line with the waste produced by a laboratory based HPLC which require specialist disposal. Grade 5 represents the ideal aim of a portable HPLC: < 100 mL/day non-hazardous waste disposed of in ordinary waste or recycling streams. To date, many prototypes report low waste production in line with Grade 4; however, no systems are yet to report non-hazardous waste production.

2. BETTER Criteria radar charts for systems reviewed in this work

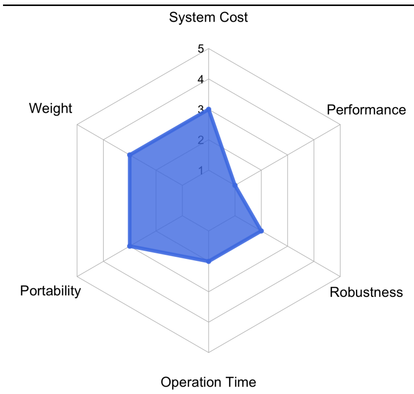
Otagawa et al. (1986)	Baram et al. (1996)	Tulchinksy, St. Angelo (1998)

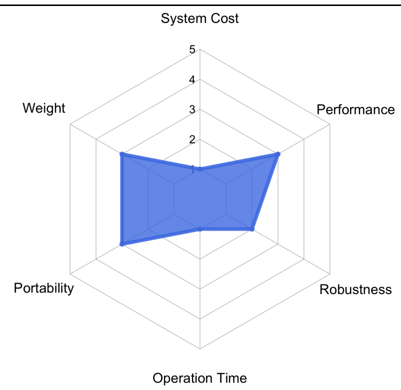


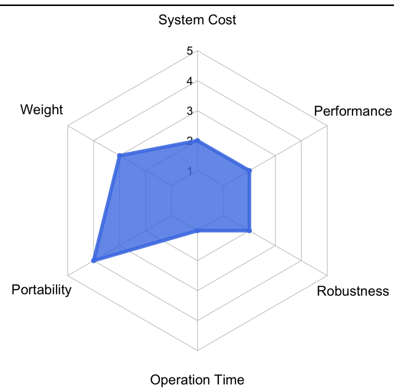




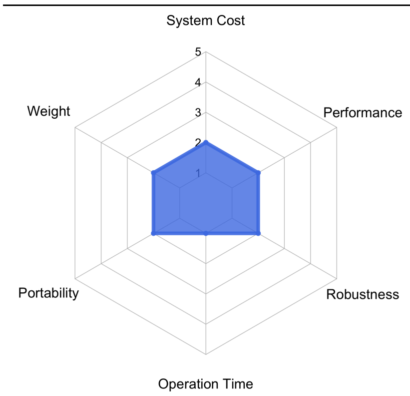
Ishida et al. (2015)	Sharma et al. (2015)	Li et al. (2015)

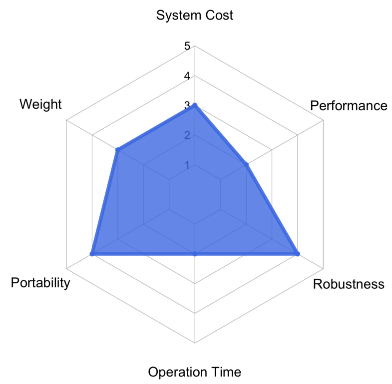


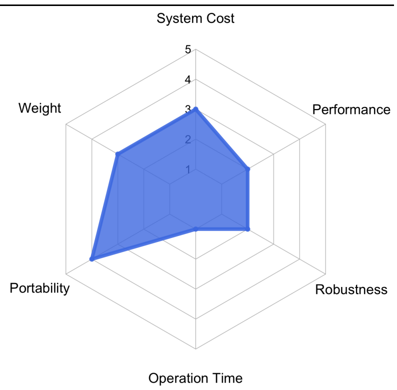




Lynch et al. (2017)	Chatzimichail et al. (2019)	Lam et al. (2020)







3. Breakdown justification of BETTER criteria grades for systems reviewed in this work

Prototype	BETTER criteria		Justification
Otagawa et al.[1]	**System Cost**	1	The cost of the system was not discussed; however, it is likely that the cost of the prototype was similar to (and exceeded) a commercial, laboratory-grade HPLC system at the time of publication. Similarly, it is unlikely that affordable, miniaturised components were available. Therefore, the prototype likely comprised of customised parts. The weight, size, operation time, and robustness of the prototype were not discussed; however, given the decade in which the system was reported, it is highly likely that the system was similar to a laboratory HPLC system with respect to the above factors. The chromatographic capability of the instrument is limited by the low attainable pressure (<10 bar).
	Weight	1	
	Portability	1	
	Operation time	1	
	Robustness	1	
	Performance	1	
Baram et al.[2]	**System Cost**	1	The cost of the system was not discussed; however, it is likely that the cost of the prototype was similar to a commercial, laboratory-grade HPLC system. Similarly, it is unlikely that affordable, miniaturised components were available. Therefore, the prototype likely comprised of expensive, custom parts. The weight and size of the prototype were given a score of 1 each. This is because the prototype would require a robust power supply for use in the field. A petrol generator (Böhmer-AG 6500W, Petrol Generator, 3.4kVA, 8Hp With UK Plugs) weighs 40 kg empty. It can run for circa. 16h on 11L of petrol; Petrol weighs 0.7489 g/cm^3 (aqua-calc.com); 11L petrol is 8.29 kg. Therefore, the overall weight and size of the prototype, taking into account externalities would be considerably greater than that of the prototype alone. The operation time, and robustness of the prototype were not discussed; however, given the decade in which the system was reported, it is highly likely that the system was similar to a laboratory HPLC system with respect to the above factors. The prototype was reported to achieve a maximum pressure of 70 bar.
	Weight	1	
	Portability	1	
	Operation time	1	
	Robustness	1	
	Performance	2	

Tulchinsky, St. Angelo[3]	**System Cost**	1	The cost of the system was not discussed; however, it is likely that the cost of the prototype was similar to a commercial, laboratory-grade HPLC system. Similarly, it is unlikely that affordable, miniaturised components were available. Therefore, the prototype likely comprised of expensive, custom parts. It is worth mentioning that the reported size and weight of Minichrom does not account for the solvent reservoirs, computer and battery necessary for its operation. The prototype requires a lead-acid battery for operation; typically, these weigh 15 kg alone. The prototype along with the necessary battery, solvent/waste reservoirs, and battery are able to be transported in a standard vehicle. 8 hours operation time is equivalent to one working day. The system is enclosed in an aluminium case reported to be capable of withstanding shocks and vibrations common in field testing. Since there were no published results of mechanical stability or impact analysis for Minichrom, the robustness of the system was not confirmed. The system is capable of up to 350 bar using an isocratic configuration.
	Weight	1	
	Portability	2	
	Operation time	1	
	Robustness	2	
	Performance	3	
Ishida et al.[4]	**System Cost**	3	Microfluidic-chip based column and detector can be relatively low cost depending on the materials used. Although this does not take into account the initial capital cost for the equipment required in fabricating the microfluidic chip. The prototype can be considered briefcase sized once externalities are accounted for. The operation time is reported as up to 24 hours on batteries according to authors. The stability of the portable LC within a field environment was not part of the tests conducted with this device. An issue that may be encountered is related to the stability of the EOP in response to shocks and vibrations. Therefore, it is reasonable to assume that the system cannot be operated during transportation. The performance of the system is limited by the electroosmotic pump (<10 bar).
	Weight	3	
	Portability	3	
	Operation time	2	
	Robustness	2	
	Performance	1	

Sharma et al.[5]	**System Cost**	1	While the cost of the prototype was not discussed, the pumping system employed is a custom design from VICI Valco Instruments (Houston, TX, USA); this is likely to be expensive and where the bulk of the prototype cost lies. Once externalities including computer, batteries, and a temperature control device are incorporated, the overall prototype will likely weigh between 3-10 kg, and will be the size of a briefcase. The system was battery-operable using a 10 A-h 24 V DC battery capable of powering the device for up to 8 hours. This is equivalent to one working day. The prototype is unlikely to withstand operation during transportation since shock impacts may disturb the alignment of the on-column detector. Gradient enabled system capable of pressures up to 550 bar.
	Weight	3	
	Portability	3	
	Operation time	1	
	Robustness	2	
	Performance	3	
Li et al.[6]	**System Cost**	2	This was the first system to disclose any equipment costs; however, this was quoted for the syringe pump module alone ($6,871). Incorporating costs for all componentry will likely raise this to above $10k. The weight of the syringe pump module is reported to be 1.3 kg. The weight of the system overall is unknown since this does not include the weight of a battery, computer, or data acquisition modules and detector module. It is likely that the weight of the overall system will be 3-10kg with the addition of these componentry. The dimensions of the Labsmith LC platform (25 cm x 25 cm - L x W) allow the prototype to comfortably fit inside a small backpack with all externalities. The operation time of the prototype was not discussed. However, it is reasonable to assume that the system components can be operated using a standard battery for at least a full working day. The robustness of the prototype was not discussed. However, given the size of the prototype, one can speculate that the system can withstand shocks and vibrations during transportation with adequate housing. Gradient enabled system capable of pressures up to 115 bar.
	Weight	3	
	Portability	4	
	Operation time	1	
	Robustness	2	
	Performance	2	

Lynch et al.[7]	**System Cost**	2	The HPLC cartridge was described as low-cost. However, the cost of the prototype was not discussed. In addition, the detector was not incorporated, therefore, the full cost of the prototype can only be estimated and likely to be grade 1 if this includes the MS system. The HPLC cartridge does not incorporate a detector or a computer (required for controlling the system and powering the cartridge). These will likely increase the weight of the system up to 10 kg depending on the type of detector used. A UV-vis detection system will likely add up to 1 kg depending on capability; however, a field-transportable mass spectrometer would weigh approximately 32 kg (https://www.rightek.com.tw/product_pdf/185/Microsaic-4500-Brochure.pdf) and only be *transportable*, not portable. Depending on the chosen detection system, the prototype will likely need to be transported using a non-specialist vehicle. The operation time of the prototype was not discussed. However, it is reasonable to assume that the system components can be operated using a standard battery for at least a full working day assuming the use of low power LEDs as part of the detector. The robustness of the prototype was not discussed. However, given the size of the prototype, one can speculate that the system can withstand shocks and vibrations during transportation with adequate housing. Gradient enabled system capable of pressures up to 140 bar.
	Weight	2	
	Portability	2	
	Operation time	1	
	Robustness	2	
	Performance	2	
Chatzimichail et al.[8]	**System Cost**	3	The system cost was not discussed. The inexpensive nature of the pre-pressurised gas pump contributes to the low cost of the device below $10k. The prototype weighed 6.7 kg with all requisite computer systems, battery units, and solvents fully integrated. The HPLC instrument reported was a completely standalone system in a briefcase-style enclosure. Battery operation typically allows for operation times of 13 hours. Chatzimichail et al. performed several drop tests from a vertical height of 1 m while the device was operating. These tests confirmed the stability and ruggedness of the device to impact shocks, since there was negligible divergence in the baseline noise prior to and following impact. Isocratic elution demonstrated with pressures of up to 150 bar.
	Weight	3	
	Portability	4	
	Operation time	2	
	Robustness	4	
	Performance	2	

Lam et al.[9]	**System Cost**	3	This follow-up prototype to Li et al.'s system also uses Labsmith components, incorporating a detection system, battery, data acquisition modules, and 3D printed housing. Given the simplification of the instrumentation in contrast to the previous prototype, it is likely that the overall system, including the above externalities, would cost below $10k. The system weight (2.7 kg) does not account for externalities such as the computer. This will likely increase the overall weight to above 3 kg. Given the dimensions of the 3D printed housing (24.5 cm x 18.5 cm x 16.0 cm - L x W x H), it is suitable to assume that the prototype would fit within a small backpack. While the operation time of the system was not mentioned, the authors specified that a 24000 mAh portable battery powers the prototype. It is reasonable to assume that this would provide power for a full working day. Without further information regarding the power consumption of the components, no further estimations can be made. The robustness of the prototype was not discussed. However, given the size of the prototype, one can speculate that the system is resistant to transportation due to adequate housing. Gradient enabled system capable of pressures similar to previous prototype by Li et al.
	Weight	3	
	Portability	4	
	Operation time	1	
	Robustness	2	
	Performance	2	

References

1. Otagawa T, Stetter JR, Zaromb S (1986) Portable liquid chromatograph for analysis of primary aromatic amines in coal-derived materials. J Chromatogr A 360:252–259. https://doi.org/10.1016/S0021-9673(00)91671-6

2. Baram GI (1996) Portable liquid chromatograph for mobile laboratories I. Aims. J Chromatogr A 728:387–399. https://doi.org/10.1016/0021-9673(95)01271-0

3. Tulchinsky VM, St. Angelo DE (1998) A practical portable HPLC system - MINICHROM, a new generation for field HPLC. F Anal Chem Technol 2:281–285. https://doi.org/10.1002/(SICI)1520-6521(1998)2:5<281::AID-FACT5>3.0.CO;2-V

4. Ishida A, Fujii M, Fujimoto T, et al (2015) A Portable Liquid Chromatograph with a Battery-operated Compact Electroosmotic Pump and a Microfluidic Chip Device with a Reversed Phase Packed Column. Anal Sci 31:1163–1169

5. Sharma S, Plistil A, Barnett HE, et al (2015) Hand-Portable Gradient Capillary Liquid Chromatography Pumping System. Anal Chem 87:10457−10461. https://doi.org/10.1021/acs.analchem.5b02583

6. Li Y, Dvořák M, Nesterenko PN, et al (2015) Miniaturised medium pressure capillary liquid chromatography system with flexible open platform design using off-the-shelf microfluidic components. Anal Chim Acta 896:166–176. https://doi.org/10.1016/j.aca.2015.09.015

7. Lynch KB, Chen A, Yang Y, et al (2017) High-performance liquid chromatographic cartridge with gradient elution capability coupled with UV absorbance detector and mass spectrometer for peptide and protein analysis. J Sep Sci 40:2752–2758. https://doi.org/10.1002/jssc.201700185

8. Chatzimichail S, Casey D, Salehi-Reyhani A (2019) Zero electrical power pump for portable high-performance liquid chromatography. Analyst. https://doi.org/10.1039/C9AN01302D

9. Lam SC, Coates LJ, Hemida M, et al (2020) Miniature and fully portable gradient capillary liquid chromatograph. Anal Chim Acta 1101:199–210. https://doi.org/10.1016/j.aca.2019.12.014